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Jumada Al-Thani 1411

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ANNALS of Saudi Medicine

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Publications Office
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Indexed by Current Contents, Excerpta Medica,
and Current Awareness in Biological Sciences.
ISSN 0256–4947

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ANNALS OF SAUDI MEDICINE

Aims and Scope

The *Annals of Saudi Medicine* is a joint project of the King Faisal Specialist Hospital and Research Centre and the King Saud University College of Medicine and King Khalid University Hospital. The journal is typeset and printed at the King Saud University Press, Riyadh, Saudi Arabia. Since July 1985, the *Annals* has incorporated *The King Faisal Specialist Hospital Medical Journal*, established in 1980.

The *Annals* is a bimonthly multidisciplinary medical journal. High-quality papers, written in English, dealing with aspects of clinical, academic or investigative medicine or research will be welcome. Emphasis is placed on matters relating to medicine in Saudi Arabia in particular, and the Middle East in general, though articles are welcome from anywhere in the world, and the *Annals* has worldwide readership.

The *Annals* publishes original articles, case reports, letters to the editor, editorials, and from time to time, special communications, commentaries, and review articles. Abstracts of meetings and symposia sponsored by the Joint Board for Postgraduate Medical Education of Saudi Arabia are published, and the proceedings of such symposia may be published if the Editorial Board considers them appropriate and relevant. The Editorial Board wishes to minimize delay between manuscript submission, decision, and publication, and accordingly authors are requested to follow carefully the instructions set out under "Information for Authors."

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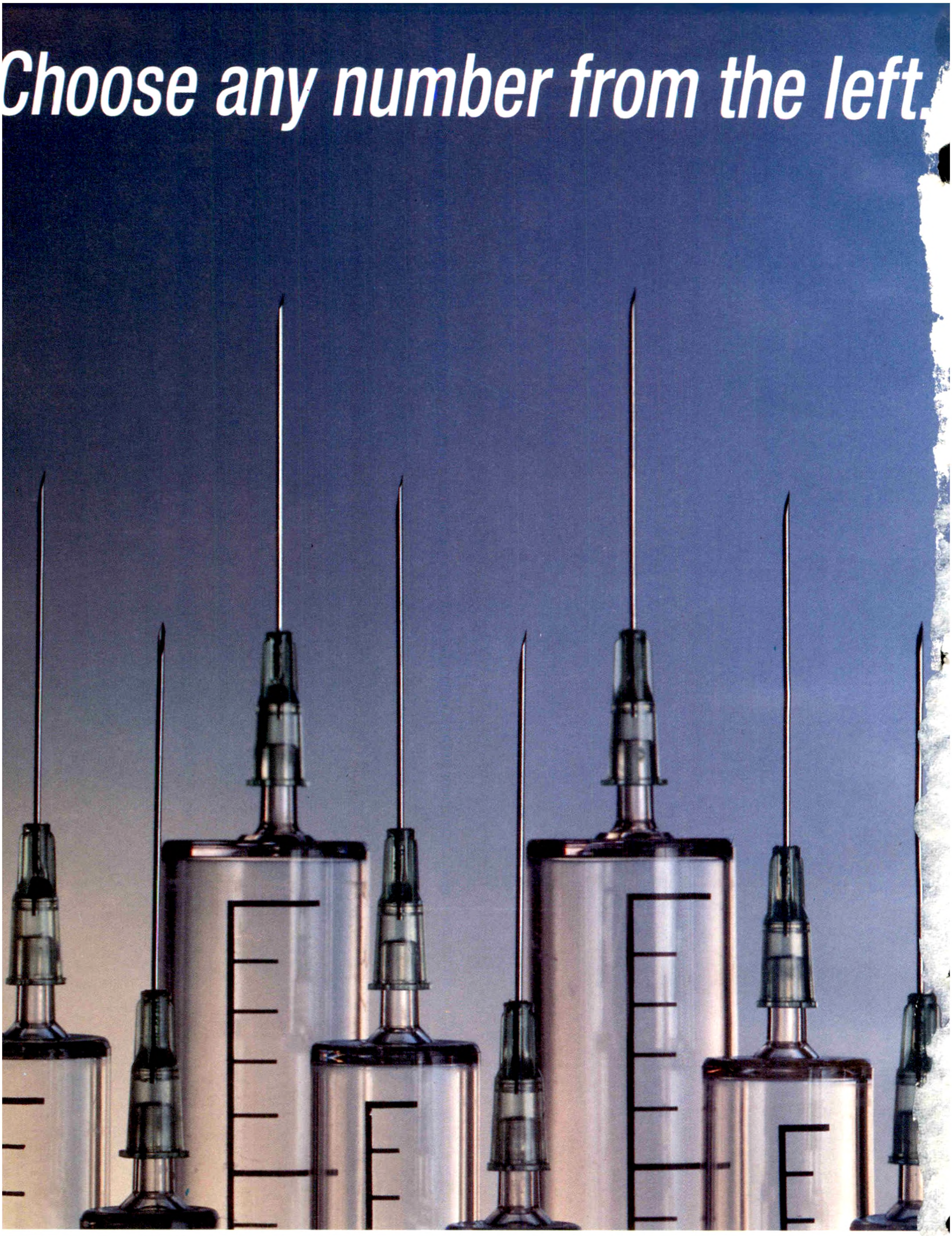
* See: International Code of Marketing of Breast Milk Substitutes, adopted by the World Health Assembly in Resolution WHA 34.22, May 1981.



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urticarial rash suggests penicillin hypersensitivity and treatment should be discontinued. Erythematous rashes are frequently mild and transient but may be severe when associated with infectious
ucleosis, in which case treatment should be discontinued. Rare cases of erythema multiforme, Stevens-Johnson syndrome and an occasional case of exfoliative dermatitis have been reported
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Further information is available on request from SmithKline Beecham Pharmaceuticals International, Brentford, England. AUGMENTIN is a product of research from
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Mothers should be given guidance on the preparation for, and maintenance of, lactation, with special emphasis on the importance of a well-balanced diet both during pregnancy and after delivery. Unnecessary introduction of partial bottle-feeding or other foods and drinks should be discouraged since it will have a negative effect on breastfeeding. Similarly, mothers should be warned of the difficulty of reversing a decision not to breast-feed.

Before advising a mother to use an infant formula, she should be advised of the social and financial implications of her decision: for example, if a baby is exclusively bottle-fed, more than one can (450 g) per week will be needed, so the family circumstances and costs should be kept in mind. Mothers should be reminded that breast-milk is not only the best, but also the most economical food for babies.

If a decision to use an infant formula is taken, it is important to give instruction on correct preparation methods, emphasizing that unboiled water, unboiled bottles or incorrect dilution can all lead to illness.

* See International Code of Marketing of Breast Milk Substitutes, adopted by the World Health Assembly in Resolution WHA 34.22, May 1981

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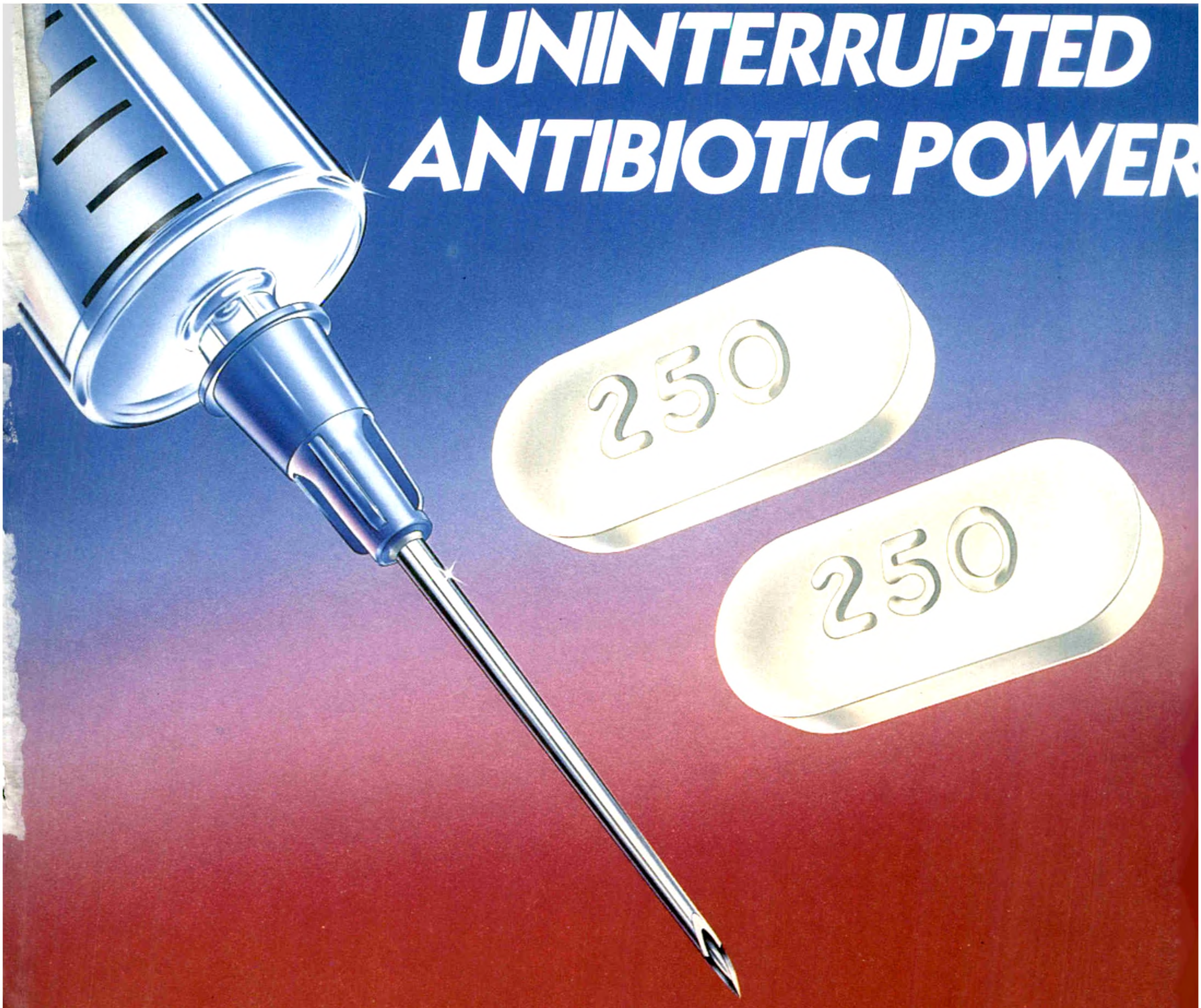

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tes). *Prophylaxis:* The usual dose of 1.5g i.v. with induction of anaesthesia for abdominal, pelvic and orthopaedic
may be supplemented with two 750mg i.m. doses 8 and 16 hours later. In cardiac, pulmonary, oesophageal and
erations, the usual dose is 1.5g i.v. with induction of anaesthesia continuing with 750mg i.m. t.i.d. for a further
urs. In total joint replacement, 1.5g cefuroxime powder may be mixed dry with each pack of methyl methacrylate
lymer before adding the liquid monomer. **Contra-indication:** Hypersensitivity to cephalosporins.
s: Cephalosporins may, in general, be given safely to patients who are hypersensitive to penicillins. Care is
patients who have experienced an anaphylactic reaction to penicillin. As with all drugs, Zinacef should be
d with caution during the early months of pregnancy. Zinacef should not be mixed in the syringe with
side antibiotics. Reduce dosage when renal function is markedly impaired. (See data sheet for details.)
rins at high dosage should be given with caution to patients receiving concurrent treatment with potent diuretics
isemide, as these combinations are suspected of adversely affecting renal function. Clinical experience with
shown that this is not likely to be a problem at the recommended dose levels. **Side effects:** Adverse reactions are
enerally mild and transient, e.g., hypersensitivity reactions (rashes and rarely anaphylaxis), gastro-intestinal
es, decreased haemoglobin concentration, eosinophilia, leucopenia, neutropenia and a positive Coombs' test.
ses in serum liver enzymes. Transient pain after i.m. injection. As with other antibiotics, prolonged use may result
rowth of non-susceptible organisms, e.g. Candida. **Package quantities:** Zinacef 250mg or Zinacef 750mg (for
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dose. *Children:* Most infections – 125mg twice daily. Otitis media – 250mg twice daily. Tablets should not be chewe
crushed and therefore are not suitable for children under five years of age. ZINNAT should be taken after food for optim
absorption. **Contra-indications** Hypersensitivity to cephalosporin antibiotics. **Precautions** ZINNAT may in general be g
safely to patients who are hypersensitive to penicillins, although cross-reactions have been reported with s
cephalosporins and special care is indicated in patients who have experienced anaphylactic reaction to penicil
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disturbances including diarrhoea, nausea and vomiting have been reported, these are generally mild and transient in nat
As with all broad spectrum antibiotics, there have been rare reports of pseudomembranous colitis. Rarely, hypersensit
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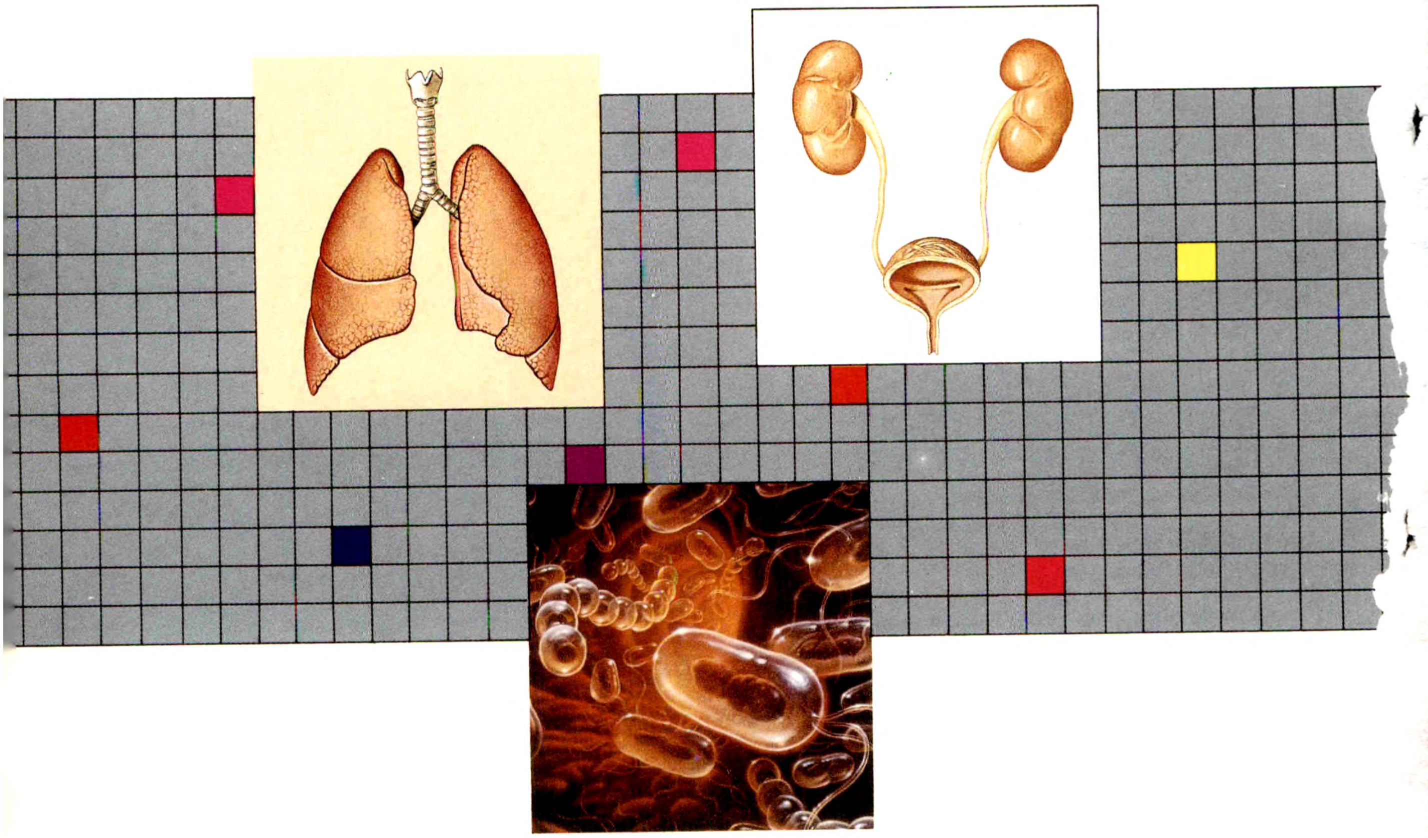

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Confidence

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Most hospitalised patients are to some degree immunocompromised and are therefore at special risk of infection.

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- old age
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- catheters

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Presentation: Fortum for injection is supplied in vials containing 250 mg, 500 mg, 1 g and 2 g ceftazidime (as pentahydrate) with sodium carbonate. **Uses:** Fortum is a bactericidal cephalosporin in antibiotic which is resistant to most beta-lactamases and is active agains a wide range of Gram-positive and Gram-negative bacteria. It is indicated for the treatment of single infections and for mixed infections caused by two or more susceptible organisms. Fortum, because of its broad antibacterial spectrum, may be used alone as first choice dru pending sensitivity test results. **Dosage and administration:** *Adults:* 1 g to 6 g i.m. or i.v. per day and by the i.p. route 125 to 250 mg per two litres of dialysis fluid (see Data Sheet for details). *Neonates, Infants and Children:* Up to two months: 25 to 60 mg/kg/day given a two divided doses has proved to be effective. In the neonate the serum half-life of ceftazidime can be three to four times that in adults. Over two months: 30 to 100 mg/kg/day given as two or three divided doses (see Data Sheet for details). In Impaired Renal Function: th dosage of ceftazidime should be reduced when the glomerular filtration rate (GFR) falls below 50 ml/min. An initial loading dose of 1 g may be given to patients with suspected renal insufficiency (see Data Sheet for details). **Contra-indication:** Fortum is contra-indicated i patients with known hypersensitivity to cephalosporin antibiotics. **Precautions:** Cephalosporins may, in general, be given safely to patients who are hypersensitive to penicillins. Care is indicated in patients who have experienced an anaphylactic reaction to penicillin. Cephalospori antibiotics at high dosage should be given with caution to patients receiving concurrent treatment with nephrotoxic drugs. Clinical experience with Fortum has shown that this is not likely to be a problem at the recommended dose levels. As with all drugs, Fortum should b administered with caution during the early months of pregnancy and in early infancy. Fortum is excreted in human milk in low concentrations. Fortum does not interfere with enzyme-based tests for glycosuria. Slight interference with copper reduction methods may be observe Fortum does not interfere in the alkaline picrate assay for creatinine. Fortum and aminoglycosides should not be mixed in the same giving set or syringe. As with other broad spectrum antibiotics, prolonged use of Fortum may result in the overgrowth of non-susceptible organisms (e.g., Candida, Enterococci) which may require interruption of treatment or adoption of appropriate measures. **Side effects:** Fortum is generally well tolerated with only infrequent adverse reactions, e.g. pain and/or inflammation after i.m. administration and phlebitis and/or thrombophlebitis after i.v. administration, rashes, fever, pruritus, anaphylaxis, gastrointestinal disturbances, headache, dizziness, paraesthesia and bad taste. Transient changes in laboratory values may occur including: eosinophilia, a positive Coombs' test, thrombocytosis, leucopenia, thrombocytopenia and slight rises in hepatic enzymes.

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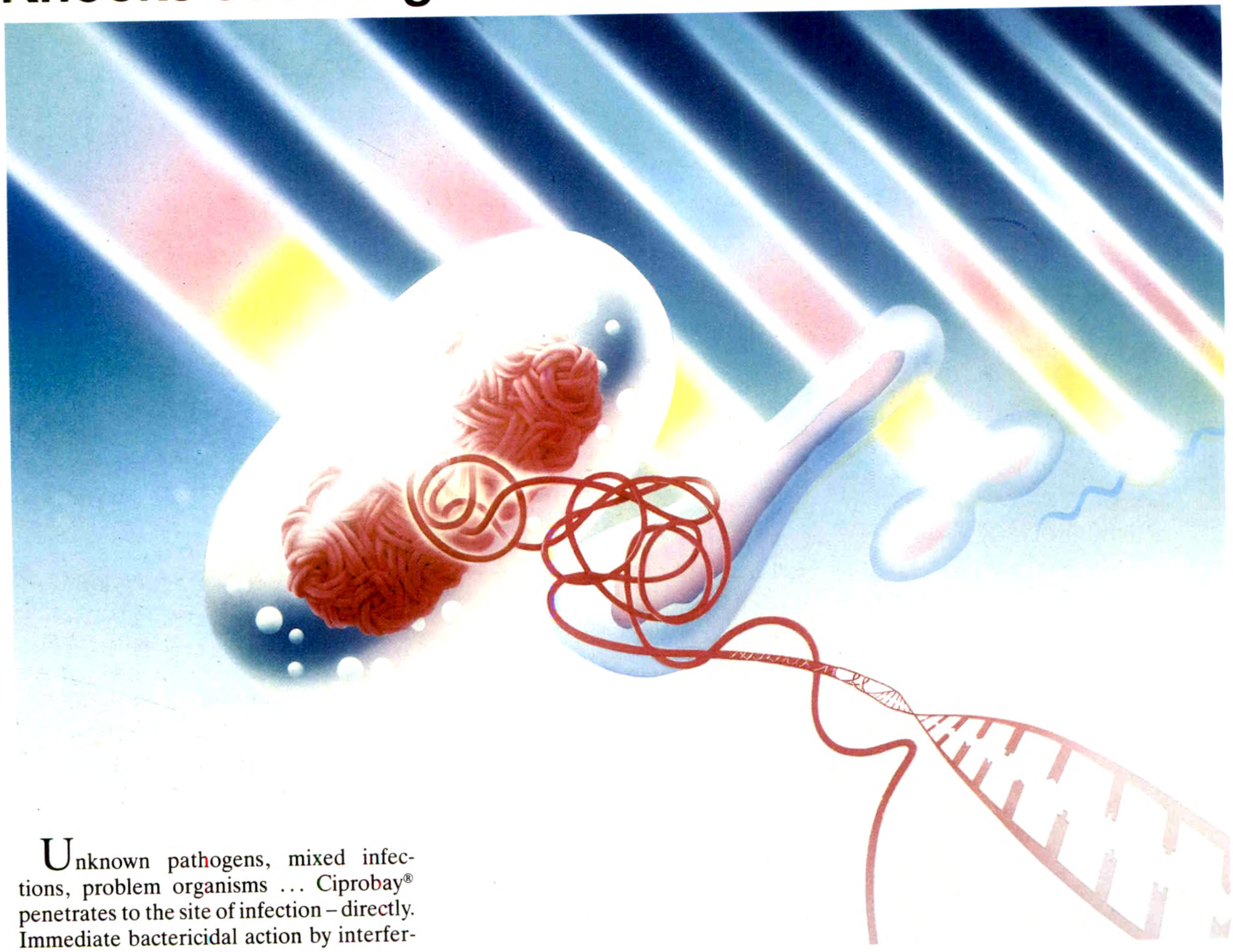

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Editorial

THE PLACE OF OBJECTIVE STRUCTURED CLINICAL EXAMINATIONS IN UNDERGRADUATE AND POSTGRADUATE MEDICINE

This issue of the *Annals of Saudi Medicine* contains an interesting article by Dr. Abdullah Mohamed Abo-Bakr on the role of Objective Structured Clinical Examinations (OSCE) in the assessment of clinical competence of medical students [1]. Briefly the concept involves a series of clinical (patient-based) stations alternating with written question stations. Candidates progress around the circuit of stations, completing the task at each one in an allotted time. An examiner at each clinical station marks each candidate's performance, using a predetermined marking schedule. At the written question stations no examiner is present, and the candidate completes various tasks based on written material, photographs, x-rays, laboratory reports, etc., which may relate to the clinical problem at the previous station. All candidates pass through all stations.

Whilst this method of assessment of clinical competence emanated from Scotland in 1975 [2], the approach of having medical student examinations based on a circuit of stations has been used in some medical schools for many years. For example, it was used in subjects such as anatomy, physiology, pathology, and microbiology at Northwestern University Medical School, Chicago, in the 1960s. Experience with the basic system has repeatedly shown a degree of efficiency and time saving during the actual examination, balanced by an awful lot of work in preparing the examination—something akin to the work which lies behind each good multichoice question (MCQ).

Also akin to some of the disadvantages of MCQ, the OSCE deals with vignettes, with parts, rather than the whole. Thus, the capacity to give a coherent written account of the pathology of diabetes mellitus is not tested by a few MCQs—similarly, a station with a patient with a diabetic gangrenous foot does not test the candidate's overall competence to diagnose and manage diabetes. However, advantages of OSCE include the possibility of immediate student feedback, and good interrelated involvement between student and teacher.

At the postgraduate level, too, there are developments involving OSCE. At a recent meeting of the Royal New Zealand College of General Practitioners, a workshop on the topic evoked much interest [3]. Participants found that the most educationally fertile ground was in constructing a clinical OSCE station, rather than using it to test a candidate. The 30 or so workshop participants, all experienced family practitioners, were divided into six groups and asked to work out the essential elements of a common general practice situation, viz., a fit young woman presenting to her family practitioner requesting for the first time a prescription for oral contraceptives.

Groups were asked to list elements of history taking, physical examination, advice and instructions in two categories—essential and important. When the six groups reassembled, it was apparent that what one group of experienced doctors considered essential, another group deemed far less important.

The next step in the workshop was to put the questions to the test. In each group, one doctor was asked to be the patient, another to be the doctor, and the rest to be observers. Only the advice and instructions part of the consultation was to be covered, as the second 7½-minute part of this simulated 15-minute consultation. In all groups, it was quickly apparent that the list of so-called essentials was far too much to be digested by the patient. Thus was demonstrated a mismatch between textbook medicine and the reality of dealing with a patient in a particular setting, in this case general practice.

Other postgraduate educational examples could include a patient with a single swollen joint; a woman presenting with irregular vaginal bleeding; or a case of sudden unexpected death.

From Dr. Abo-Bakr's article, it is apparent that there is a place for the OSCE in medical schools, and as experience with this valuable assessment tool develops, it may also find an important role in postgraduate continuing medical education.

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Original Articles

EFFECT OF INITIAL ISONIAZID RESISTANCE ON RESPONSE TO CHEMOTHERAPY OF TUBERCULOSIS: A REVIEW OF CLINICAL TRIALS

Ibrahim O. M. Al-Orainey, MRCP(U.K.)

جرى تقييم سبع عشرة محاولة سريرية لاستخدام دورات قصيرة من المعالجة الكيميائية للدرن وذلك لدراسة تأثير المقاومة الأولية للآيسونيازيد على الاستجابة للعلاج. لوحظ ارتفاع نسب الفشل للدورات غير المحتوية على الريفامبيسين. أما الدورات المحتوية على الريفامبيسين فقد كانت الاستجابة لها جيدة جدًّا لدى كل من المرضى المصابين بذراري مقاومة أو حساسة على السواء. وأعطت الدورات المحتوية على الريفامبيسين والبيرازيناميد أفضل النتائج إذا لوحظ انخفاض نسب الفشل لدى المصابين بذراري حساسة أو مقاومة. لكن إضافة الاستريبتومايسين والايثامبوتول لهذه الدورات لم يحسّن من استجابة المصابين بعصيات مقاومة للآيسونيازيد. أعطت إطالة فترة العلاج استجابة أفضل بشكل عام ولكن بالنسبة للدورات المحتوية على الريفامبيسين فان استعمال البيرازيناميد لأكثر من شهرين لم يغير من نتيجة العلاج. وأعطت الدورات الحاوية على الريفامبيسين والبيرازيناميد لمدة ٤ شهور و٦ شهور نسب فشل منخفضة لدى المصابين بذراري مقاومة للآيسونيازيد. وكان تأثير المقاومة الأولية للأيسونيازيد على الاستجابة لهذه الدورات قليل جدًّا حين استمر العلاج لمدة ٦ شهور.

This study evaluated seventeen clinical trials of short-course chemotherapy of tuberculosis and assessed the influence of initial resistance to isoniazid on the response to therapy. High failure rates were observed for the non-rifampicin–containing regimens. When rifampicin was included, there was a very good response among patients suffering from sensitive and resistant strains. Regimens that included both rifampicin and pyrazinamide yielded the best results, with low failure rates observed for sensitive and resistant patients. The addition of streptomycin and ethambutol to these regimens did not improve the response in patients with isoniazid-resistant bacilli. Prolonged therapy generally yielded a better response; however, in rifampicin-containing regimens, the use of pyrazinamide for more than two months did not influence the outcome of therapy. In patients with isoniazid-resistant strains, 4- and 6-month regimens containing rifampicin and pyrazinamide both yielded low failure rates. Initial isoniazid resistance had very little impact on the response to such regimens when therapy was carried out for 6 months.

Resistance of mycobacteria to antituberculous drugs is a common problem in many parts of the world. High rates of resistance have been reported from Egypt (34%), India (26%), and Thailand (52%) while low rates have been reported from Finland (2%), the U.K. (5%), and the U.S.A. (7%) [1]. The overall rate of resistance to antituberculous drugs in Saudi Arabia ranges between 13 and 21% [2,3]. Isoniazid resistance is the most common, and reflects the widespread use of the drug in the initial treatment for tuberculosis. Initial isoniazid resistance was associated with a high failure rate in clinical trials conducted in Madras and East Africa [4,5]. The advent of short-term chemotherapy which included potent drugs such as rifampicin led to a remarkable improvement in response with success rates approaching 100% [6]. This study evaluated how

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Accepted for publication 5 February 1990.

initial resistance to isoniazid influenced the response to short-course chemotherapy in patients with pulmonary tuberculosis.

Patients and Methods

This study reviewed the clinical trials of short-course chemotherapy of pulmonary tuberculosis which were conducted over the past 16 years in Africa (Kenya, Tanzania, Uganda, Zambia, Algiers), Asia (Hong Kong, Singapore, Japan), and Europe (United Kingdom and Poland) in collaboration with the British Medical Council, British Thoracic Association, and Centers for Disease Control (USA) [7–24]. In assessing these trials, information obtained included the numbers of patients sensitive to all drugs and those resistant to isoniazid, drugs used in the regimens, duration of therapy, and response to treatment. All the trials used standard methods for culturing, identifying, and testing the susceptibility of mycobacteria. Resistance to isoniazid was defined in most trials as the growth of 20 or more colonies in a medium containing 0.2 mg/L of isoniazid. A few trials defined isoniazid resistance as growth on the drug-containing medium (0.2 mg/L of isoniazid) of at least 1% more than that on the drug-free medium.

In the above trials, a failure (including relapse) was usually defined as the existence of at least two positive cultures in the last three months of treatment or in any consecutive 3 months in the 2 years after therapy.

Results

Seventeen clinical trials of antituberculous therapy were evaluated [7-24]. These trials included 7764 patients with sensitive organisms and 446 patients with isoniazid-resistant mycobacteria. The failure rate among patients with sensitive strains ranged from 1 to 30%, while patients with isoniazid-resistant strains had a failure rate ranging between 0 and 75%. The response to therapy was influenced mainly by the number and type of drugs used and the duration of therapy.

Influence of individual drugs

Streptomycin. Patients treated with streptomycin and isoniazid (6SH) exhibited a failure rate of 18%; however, the failure rate in those with an initial resistance to isoniazid was 66% (Table 1). The addition of streptomycin to rifampicin and isoniazid (6SHR) had a moderate influence on response, as failure rates among patients with sensitive strains fell from 7 to 4% and among the isoniazid-resistant group from 20 to 12%. Adding streptomycin to regimens containing both rifampicin and pyrazinamide (for 6 months) did not seem to affect the outcome of therapy (see Table 1).

TABLE 1. *Effect of inclusion of streptomycin in drug regimens on response to therapy.*

	Drug sensitive			Isoniazid resistant		
		Failures			Failures	
Drug regimens and duration (mo)	Total	No.	%	Total	No.	%
6SH	180	33	18	18	12	66
6HR	183	13	7	9	2	22
6SHR	612	26	4	35	5	14
2HRZ/4HR	225	9	4	4	0	0
2SHRZ/4HR	344	8	2	18	2	11

H = isoniazid; S = streptomycin; R = rifampicin; Z = pyrazinamide; T = thiacetazone. The number preceding the abbreviations is the duration in months

Rifampicin. The inclusion of rifampicin in therapeutic regimens has a remarkable impact on response to therapy in both sensitive and isoniazid-resistant patients. Six months' therapy with rifampicin and isoniazid (6HR) led to a failure rate of 7% among sensitive patients while two of nine patients with resistant strains failed. The addition of rifampicin to the 6SH regimen led to a reduction in the failure rate of from 18 to 3% in patients with sensitive strains and from 66 to 12% in those with isoniazid-resistant strains (Table 2). When rifampicin was added to the 6SHZ regimen, the failure rate among patients with isoniazid-resistant bacilli fell from 32% to nil.

The effectiveness of rifampicin was related to the duration of its use and whether it was combined with pyrazinamide, as shown in Table 3. A failure rate of 40% was seen in patients with isoniazid-resistant bacilli who were treated with short-term regimens not containing rifampicin; the failure rate was 16% for those whose treatment included rifampicin and that lasted for 6 months. The addition of pyrazinamide to the latter regimens reduced the failure rate to 6.3%. It is interesting to note that, when rifampicin and pyrazinamide were used, the 4- and 6-month regi-

TABLE 2. *Effect of inclusion of rifampicin in drug regimens on response to therapy.*

Drug regimens and duration (mo)	Drug sensitive			Isoniazid resistant		
		Failures			Failures	
	Total	No.	%	Total	No.	%
6HR	183	13	7	9	2	22
6SH	180	33	18	18	12	66
6SHR	612	26	4	35	5	14
6SHZ	353	54	15	38	12	32
6SHZR	150	2	1.3	7	0	0
2SHRZ/4H	258	27	10	19	12	63
2SHRZ/4HR	344	8	2	18	2	11
2SHRZ/4HZ	165	15	9	9	1	11
2SHRZ/4HZR	365	12	3	17	2	12

For abbreviations, see Table 1.

TABLE 3. *Response to chemotherapy in relation to the duration of use of rifampicin.*

Drug regimens include	Drug sensitive			Isoniazid resistant		
		Failures			Failures	
	Total	No.	%	Total	No.	%
No rifampicin	687	109	16	71	30	42
Rifampicin for 2 mo (with pyrazinamide)	640	48	7.5	33	10	30
Rifampicin for 4 mo (with pyrazinamide)	344	22	6.4	27	2	7.4
Rifampicin for 6 mo (with pyrazinamide)	1662	41	2.5	80	5	6.3
Rifampicin for 6 mo (no pyrazinamide)	955	52	5.4	55	9	16

TABLE 4. *Effect of inclusion of pyrazinamide in drug regimens on response to therapy.*

Drug regimens and duration (mo)	Drug sensitive			Isoniazid resistant		
		Failures			Failures	
	Total	No.	%	Total	No.	%
6SH	180	33	18	18	12	66
6SHZ	353	54	15	38	12	32
6HR	183	13	7	9	2	22
2HRZ/4HR	225	9	4	4	0	0
2SHRZ/4H	258	27	10	19	12	63
2SHRZ/4HZ	165	15	9	9	1	11
2SHRZ/4HR	344	8	2	18	2	11
2SHRZ/4HZR	365	12	3	17	2	12

For abbreviations, see Table 1.

TABLE 5. *Effect of inclusion of thiacetazone or ethambutol in drug regimens on response to therapy.*

Drug regimens and duration (mo)	Drug sensitive			Isoniazid resistant		
		Failures			Failures	
	Total	No.	%	Total	No.	%
6SH	180	33	18	18	12	66
6SHT	154	22	14	15	6	40
2SHRZ/4H	258	27	10	19	12	63
2SHRZ/4HT	385	27	7	21	8	38
6SHR	612	26	4	35	5	14
6SHRE	160	13	8	11	2	18
2HRZ/4HR	225	9	4	4	0	0
2HRZE/4HR	139	4	3	12	0	0

For abbreviations, see Table 1. E = ethambutol.

mens exhibited similar failure rates for patients with resistant strains.

Pyrazinamide. Pyrazinamide had a moderate influence on the outcome of therapy. When added to the 6SH regimen, it had a minimal effect among sensitive patients; however, in those with isoniazid-resistant organisms, it reduced the failure rate from 66 to 32%. Pyrazinamide was more effective when added to rifampicin-containing regimens (Table 4). Continued pyrazinamide treatment beyond 2 months in regimens that included rifampicin did not seem to improve the response to therapy. Short-term regimens using only isoniazid in the continuation phase (2SHRZ/4H) showed a 63% failure rate among isoniazid-resistant patients. When pyrazinamide was added to isoniazid in the continuation phase (2SHRZ/4HZ), only one of nine patients (11%) with isoniazid resistance exhibited failure.

Ethambutol. In most short-term chemotherapy trials, ethambutol has been used in combination with isoniazid and rifampicin with or without pyrazinamide. In such regimens, ethambutol had no influence on response to chemotherapy among sensitive or resistant patients (Table 5).

Thiacetazone. The inclusion of thiacetazone in short-term regimens had only a modest effect (Table 5). When added to the 6SH regimen, it had a minimal effect in patients with sensitive strains, but the failure rate was reduced from 66 to 40% in those resistant to isoniazid. When thiacetazone was given with isoniazid in the continuation phase of short-term therapy (2SHRZ/4TH), the failure rate among isoniazid-resistant patients remained high at 38%.

Number of Drugs Used

Regimens containing four drugs (including rifampicin and pyrazinamide) used for 6 months had very low failure rates among both sensitive and isoniazid-resistant patients. When three drugs were used for 6 months, the response was inferior to that observed for four-drug regimens and was affected mainly by the inclusion of rifampicin. Regimens that did not include rifampicin exhibited failure rates of 30 to 40% among isoniazid-resistant patients, in contrast to 12% in rifampicin-containing regimens. The findings are similar for two-drug regimens.

Duration of Therapy

In comparing similar regimens given for different durations, it appears that extending the duration of therapy from 4 to 6 or 8 months markedly improves the response in patients with sensitive strains (Table 6). These patients were treated with regimens consisting of an intensive phase of four drugs used for 2 months, followed by two or three drugs given for 2 to 6 months. The response of patients with resistant strains was affected mainly by the duration and components of the continuation phase. Patients given thiacetazone–isoniazid, isoniazid–pyrazinamide, or streptomycin–isoniazid–ethambutal combinations during the continuation phase showed a better response when this phase was prolonged. However, patients treated with isoniazid–rifampicin responded well when the drugs were given for 2 months in the continuation phase. The outcome was not improved by further prolongation of therapy. Patients with resistant bacilli who were treated with isoniazid–rifampicin for either 6 months or one year showed failure rates similar to those patients treated for 4 months (2SHRZ/2HR regimen). Therapeutic regimens that did not contain rifampicin in the initial or continuation phase were associated with high failure rates among patients with isoniazid-resistant strains. Patients treated with isoniazid–ethambutal for one year or isoniazid–thiacetazone for 18 months had failure rates of 45% and 25%, respectively.

TABLE 6. *Influence of the duration of various regimens on response to therapy.*

Drug regimens and duration (mo)	Drug sensitive			Isoniazid resistant		
		Failures			Failures	
	Total	No.	%	Total	No.	%
2SHRZ/4TH	385	27	7	21	8	38
2SHRZ/6TH	95	0	0	8	1	13
2SHRZ/2HZ	106	32	30	15	5	33
2SHRZ/4HZ	165	15	9	9	1	11
2SHRZ/2HR	190	18	9	14	1	7
2SHRZ/4HR	344	8	2	18	2	11
2SHRZ/2HRZ	79	9	11	5	1	20
2SJRZ/4HRZ	365	12	3	17	2	12
2SHRZ/4SHE	86	20	23	9	4	44
2SHRZ/6SHE	87	8	9	11	2	18

For abbreviations, see Table 1.

Discussion

Clinical trials reviewed in this paper showed that short-term chemotherapy of tuberculosis that included rifampicin and pyrazinamide were very effective among patients with sensitive and resistant strains. Data pooled from East African studies and from trials carried out in Madras showed that patients with initial isoniazid resistance, when treated with isoniazid and para-aminosalicylic acid or thiacetazone, had failure rates that ranged between 48 to 71%, compared with 14 to 28% among patients with sensitive strains [4,5]. Regimens containing rifampicin and pyrazinamide were more effective, as failure rates were only 2 to 3% in the sensitive group and 0 to 12% in patients with isoniazid-resistant strains [6–24].

Short-term three-drug regimens that did not include rifampicin, such as 6SHT or 6SHZ, led to high failure rates among isoniazid-resistant patients (32–40%) [7–9]. The inclusion of rifampicin in these regimens led to a dramatic improvement in response [8,12,15,28,21,24]. Rifampicin is a bactericidal drug with powerful sterilizing activity, and is unique among antituberculosis drugs in that it acts on slowly metabolizing (semidormant) mycobacteria [25]. Therefore, it reduced relapses and shortened the duration of therapy.

Clinical trials have shown that pyrazinamide is only moderately effective in non-rifampicin–containing regimens. Its addition to the 6SH regimen (i.e., 6SHZ) did not improve the response among patients with sensitive bacilli. However, in those with isoniazid-resistant organisms, the failure rate fell from 66 to 32% [7,9]. When pyrazinamide was added to rifampicin-containing regimens, it improved the response among patients with sensitive and resistant organisms [8,12,15,18,24]. Pyrazinamide's effects in rifampicin-containing regimens seem to stop after the initial 2 months of therapy. Prolonging its use beyond this period does not influence the outcome of therapy [15,16]. However, in non-rifampicin–containing regimens, the use of pyrazinamide after the first 2 months improved the response, particularly in patients with isoniazid-resistant organisms [18]. Pyrazinamide is a bactericidal drug that acts best in an acidic environment [25]. During the early phase of therapy, with active inflammation and phagocytosis, pyrazinamide exerts its full effects in the acidic intracellular environment. As the inflammation subsides, the medium becomes neutral and the activity of this drug decreases significantly. It is likely that regimens which include bactericidal drugs as potent as rifampicin lead to faster reduction of the inflammation and those containing less potent drugs lead to slower resolution of inflammation. This provides a suitable medium for the effects of pyrazinamide to be seen clearly. Although four-drug regimens generally resulted in a better outcome than those with two or three drugs, the actual response was related mainly to the type of drugs included in a given regimen. All four-drug regimens evaluated included rifampicin with or without pyrazinamide [17,20]. Regimens containing both drugs yielded the best results. Mitchison and Nunn [26] found that the sterilizing activity of these two drugs was not influenced by the occurrence of initial resistance. The addition of streptomycin or ethambutol to regimens containing rifampicin and pyrazinamide was not effective in patients with isoniazid-resistant organisms [8,14,17,19].

Several trials showed that prolonging a certain regimen reduced the failure rate [11,12,15,16,18]. However, for regimens that included rifampicin and pyrazinamide, patients with isoniazid-resistant bacilli were not obviously affected by prolonging therapy beyond 4 months (i.e., patients treated for 4 or 6 months had similar low failure rates) [15,16,18]. These findings reflect the powerful sterilizing activity of this combination.

Data reviewed in this study show that short-course chemotherapy containing rifampicin and pyrazinamide was very effective in patients with isoniazid-resistant mycobacteria and was almost equivalent to the outcome in those with sensitive organisms. Because of this, some investigators have questioned the value of routine pretreatment susceptibility tests on mycobacterial cultures, as the results of these tests may not lead to a change in the drug regimen [26–28]. An important exception is rifampicin resistance, because it was found to be associated with an unacceptably high failure rate [26]. Therefore, as long as rifampicin resistance remains low, the impact of initial drug resistance on antituberculous therapy is negligible.

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CONGENITAL ADRENAL HYPERPLASIA

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لا تُعرف جيدًا نسبة وقوع فرط تنسج الكظر الخِلقي ولا تواتر حالة حمل هذا الاضطراب في المملكة العربية السعودية. لكن يفترض أن يكون كلا الرقمين مرتفعين بالنظر إلى شيوع حالات الزواج من أقارب الدرجة الأولى في هذا الجزء من العالم. ونعرض هنا خمساً وعشرين حالة من حالات فرط تنسج الكظر الخِلقي، معظمها ناتج عن خلل في الأنظيم ٢١ هيدروكسيلاز، شخصت وتوبعت على مدى ثلاث سنوات في مستشفى السليمانية للأطفال في الرياض. كانت المجموعة تتكون من عشرة أولاد وخمس عشرة بنتًا ظهرت عليهم جميع درجات التذكير، غالبا من الدرجة الثالثة (٥٣٪) والدرجة الرابعة والدرجة الخامسة (١٣,٣٪ لكل منهما). كانت درجة تذكير الأعضاء التناسلية الظاهرة في البنات (٤٦٪) بارزة إلى حد أدى إلى الخطأ في تحديد الجنس إبّان الولادة لدى سبع مريضات. ونتج عن ذلك إزعاج نفسي شديد للأهل وبخاصة قبل التصحيح الجراحي. وكان تواتر وفيات الوالدان المرتبطة باضطراب مشابه مرتفعا (١٢٪) لدى عائلات المرضى. كان متوسط العمر حين بدء أزمات فقد الملح لدى الرضع المصابين ٩ أيام للاناث و ٢٥ يومًا للذكور، وكانت هذه أكثر الظواهر السريرية لهذا الاضطراب شيوعا (٨٠٪). لذا لا بد من تقصي هذا الاضطراب لدى الولدان بصورة منهجية وتشخيصه داخل الرحم لدى العائلات المعرضة له من أجل التدخل الهرموني وبالتالي الحيلولة دون تكوّن أعضاء تناسلية غامضة وتفادي ما يستتبع ذلك من جراحة رأبية لا بد من إجرائها للمريضات.

The incidence of congenital adrenal hyperplasia in Saudi Arabia and the frequency of the carrier rate are not well known. Both figures should be high, considering the commonness of first-degree consanguinity in this part of the world. We present 25 cases of congenital adrenal hyperplasia, most of them due to a defect of the 21 hydroxylase enzyme, diagnosed and followed over three years at Suleimania Children's Hospital in Riyadh. There were ten boys and 15 girls exhibiting all degrees of masculinization, mostly Grade III (53%) and Grade IV and V (13.3% each). The degree of masculinization of the external genitalia in the girls (46XX) was sufficiently pronounced in seven patients to lead to sex identity errors at birth. This aggravated the psychological reactions in the families, particularly before the surgical correction. The frequency of neonatal deaths in the patients' families related to a similar disorder was high (12%). The mean age at onset of the salt-losing crises in affected infants was 9 days in females and 25 days in males and this was the most common clinical presentation of the disorder (80%). Systematic neonatal screening and intrauterine diagnosis in at risk families must be done to provide hormonal intervention and thus prevent the formation of ambiguous genitalia and avoid the resulting plastic surgery that must be performed in female patients.

Congenital adrenal hyperplasia is common in Riyadh, where marriages between first-degree relatives are frequent. As everywhere, and particularly under the local sociocultural conditions, discussion is focused on the genetic sex which is

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Accepted for publication 17 February 1990.

not always easy to determine, depending on the degree of masculinization of otherwise genetically defined females. The surgical correction and the psychological consequences in the affected families also contribute to the problems. Intrauterine and neonatal screening are therefore important. Likewise, intrauterine treatment may prevent genital abnormalities and the neonatal deaths caused by salt-losing crises. The etiology, medical and surgical treatment, and follow-up of clinical, radiological, and biological features are discussed, along with the problems of neonatal and intrauterine screening.

Patients and Methods

Congenital adrenal hyperplasia was diagnosed in 25 patients who were followed up at the Suleimania Children's Hospital in Riyadh over a period of three years. Nationality and supposed sex as well as family history were recorded. The age of onset and clinical presentation, particularly the presence or absence of a salt-losing syndrome, and the degree of genital ambiguity were noted. Routine laboratory studies included serum urea and creatinine, electrolytes in the blood, and urine and blood gas assays as well as hormonal radioimmunoassays of 17 hydroxyprogesterone, adrenocorticotropin (ACTH), and testosterone. Hormonal radioimmunoassays of D4 androstanedione, 11 desoxycortisol, renin plasmatic activity, and HLA typing were not done. Chromosomal analysis was done in all patients. Bone age was evaluated in a left wrist/left hand x-ray study in all patients (Greulich/Pyle and Sempe Pedron Atlas).

Evaluation of the adrenal hyperplasia, the internal genitalia (in the female patients), and the rare possible tumors was documented by abdominal ultrasound and computed tomography. Genitography was done in 15 females.

Results

Among our 25 patients, 40% were male (46XY) and 60% were female (46XX). However, seven of the 15 female patients bore a male name when first seen. Ninety-two percent of the patients were Saudi and 8% were non-Saudi. Most were from Riyadh and environs (68%) (Table 1). First-degree consanguinity was found in 76% of the families. In 12% of the cases, one to two prior neonatal deaths had occurred in the family that were related to a similar disorder. The age of onset of salt losing crises in females varied from 3 to 16 days (mean, 9 days). In the males it varied from 3 days to 3 years 6 months (mean 25 days) in patients with salt loss. Among the female pseudohermaphrodite patients (46XX), 53.5% were Type III (Figures 1 and 2, Table 2) and 13.3% were Type V (Figure 3, Table 2) [1].

TABLE 1. *Patient distribution in Saudi Arabia.*

Area	Number	Percentage
Riyadh city	14	56
Riyadh region	3	12
Gassim	2	8
Jouf	1	4
Abha	2	8
Tabuk	1	4
Madinah	2	8

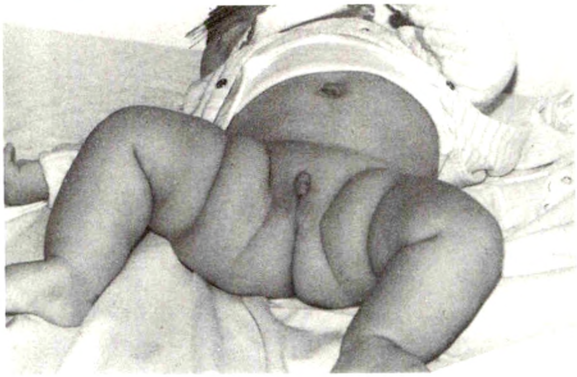

FIGURE 1. Clitoris hypertrophy, single urogenital orifice, posterior fusion of labia major (Stage III of Prader classification).

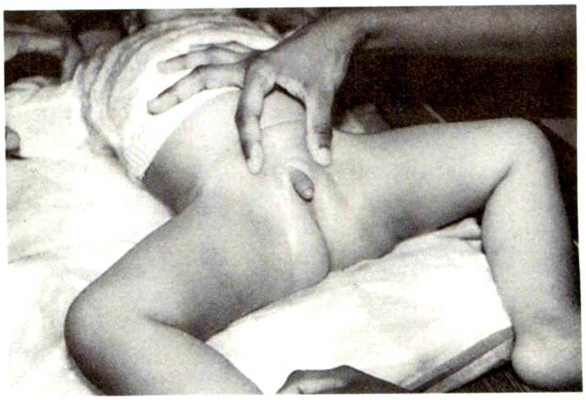

FIGURE 2. Clitoris hypertrophy, no labia fusion (Stage II of Prader classification).

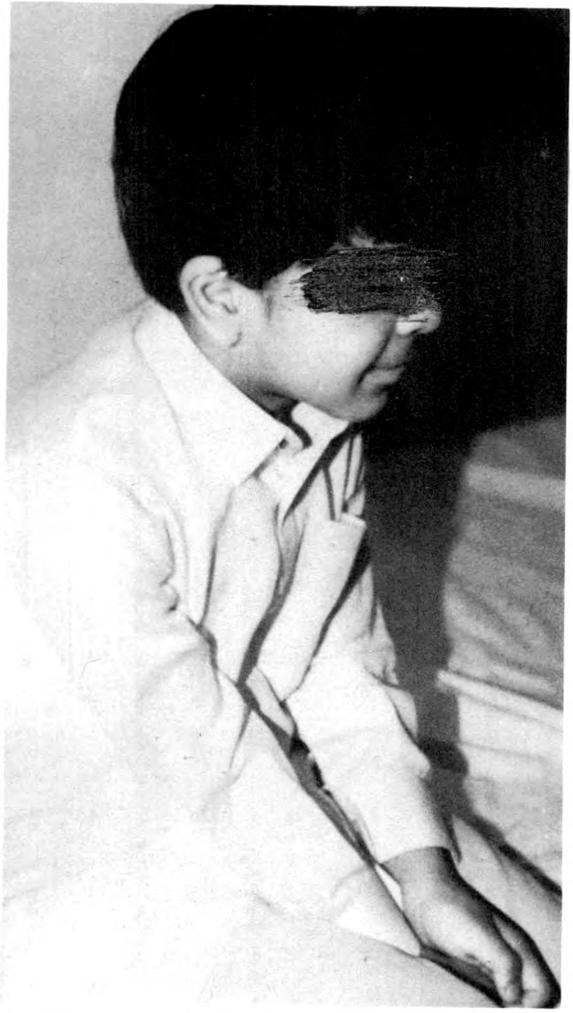

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FIGURE 3. A patient who showed complete masculinization with normal male genitalia and absence of testes, karyotype 46 XX (Stage V of Prader classification).

TABLE 2. *Prader classification.*

Classification	Cases (N=15)	Percentage
TYPE I. clitoris hypertrophy, urethral and vulvovaginal orifices present and well seen	2	13.3
TYPE II. clitoris hypertrophy, urethral and vulvovaginal orifices present but very near	1	6.6
TYPE III. clitoris hypertrophy, single urogenital orifice, partial posterior fusion of labia majora	8	53.3
TYPE IV. penile clitoris, perineoscrotal hypospadias, complete fusion of labia majora	2	13.3
TYPE V. complete masculinization (normal male-looking genitalia) but no testes	2	13.3

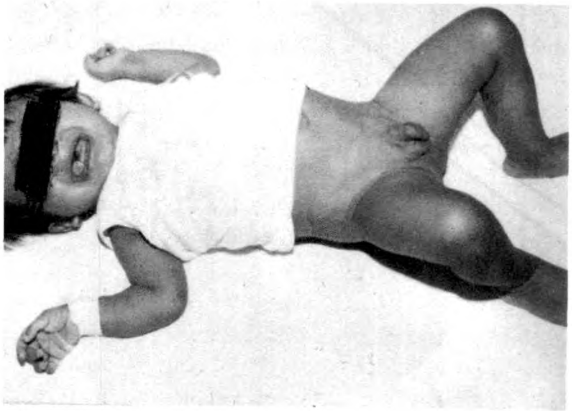

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FIGURE 4. Macrogenitosomia (big phallus, pigmented scrotum, normal testes size).

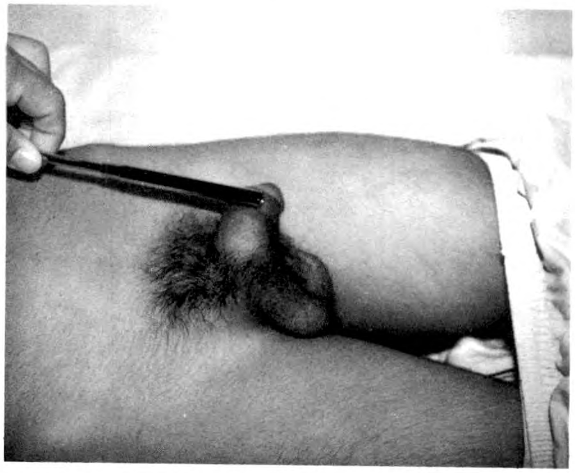

FIGURE 5. Pseudoprecocious puberty in a 3-year, 6-month-old boy (pubic hair, big phallus, normal testes size).

Among the ten male patients (46XY), only three showed virilization (big phallus, pigmented scrotum, normal testis size) at birth (Figure 4). In two patients, aged 3 years and 3 years 6 months, the initial diagnosis was "precocious puberty" (increased height, increased bone age, macrogenitosomia but normal testis size) (Figures 5,6).

The principal signs and symptoms on admission were vomiting with moderate to severe dehydration (60%) and anorexia with failure to gain weight (56%). Diarrhea occurred in 24% of the cases (Table 3).

Laboratory investigations revealed a salt-losing syndrome in 80% of the cases (20/25), with hyponatremia ranging from 126 to 106 mmol/L

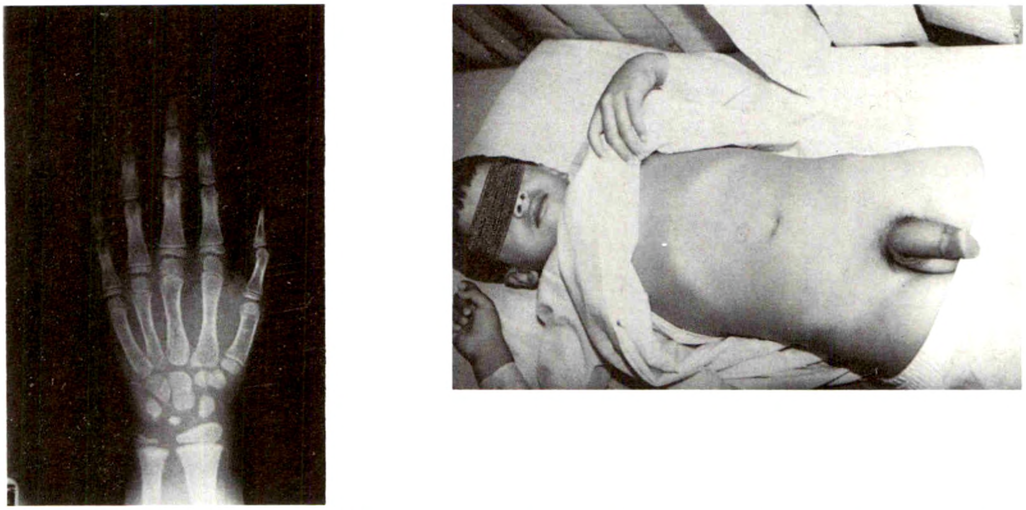

FIGURE 6. Macrogenitosomia and big phallus, pigmented scrotum, and normal testes size in a 3-year-old boy with a bone age of 8 years.

and hyperkalemia ranging from 6.5 to 10.4 mEq/L, and in 52% high urinary sodium content (mean, > 60 mmol/L in a random urine sample), moderate metabolic acidosis, and azotemia.

Hormonal radioimmunoassays showed a significantly high level of 17 hydroxyprogesterone in 23 cases (92%), high concentration of ACTH in 16 cases (64%), and high testosterone content in 12 cases (48%) (Table 4). Most of our patients (92%) had a 21 hydroxylase deficiency, as indicated by a salt loss with severe genital abnormalities and significantly high serum level of 17 hydroxyprogesterone. 17 Hydroxylase and 11 betahydroxylase deficiency are excluded, as there is no salt loss in these disorders. Conversely, patients with 3 betahydroxysteroid deshydrogenase deficiency are usually less virilized and have normal or slightly increased 17 hydroxyprogesterone levels due to hepatic 3 betahydroxysteroid deshydrogenase activity and low, normal, or sometimes slightly increased testosterone levels [2].

Bone age was advanced in almost half of the patients (12/25; 48%). Abdominal and pelvic ultrasound findings were not significant. Abdominal and adrenal computed tomography showed adrenal hyperplasia in 50% of the cases. Genitography showed vaginal hypoplasia in two cases (13.3%) and an obvious communication between the vulvovaginal cavity and vertical urethra in four cases (26.6%) (Figure 7).

TABLE 3. *Signs and symptoms.*

	Number	Percentage
Vomiting	15/25	60
Diarrhea	6/25	24
Moderate to severe dehydration	16/25	64
Anorexia and failure to thrive	14/151	56
Virilization		
Female pseudohermaphroditism	15/15	100
Macrogenitosomia		
At birth	3/10	30
After two years	2/10	20

TABLE 4. *Hormonal radioimmunoassay results.*

Hormone	Range	Mean	Normal range
17 alpha hydroxyprogesterone (ng/ml) (N = 23)	169–353	363	0.5–1
ACTH (pg/ml) (N = 16)	193–443	298	up to 90
Testosterone (nmol/L) (N = 12)	2.5–6.1	4.6	<0.5

In two patients, androgenic progestational drugs were taken by the mother during the first three months of pregnancy and their hormonal assays were within normal limits.

Treatment was conservative; initially hydrocortisone was given intravenously (10 mg/kg/day divided 6 hourly) and, after stabilization, hydrocortisone was given orally (20 to 30 mg/m^2/day). This dose was increased substantially during times of acute stress and when salt-losing crises occurred, consisting of vomiting, moderate to severe dehydration, hypotension, and metabolic

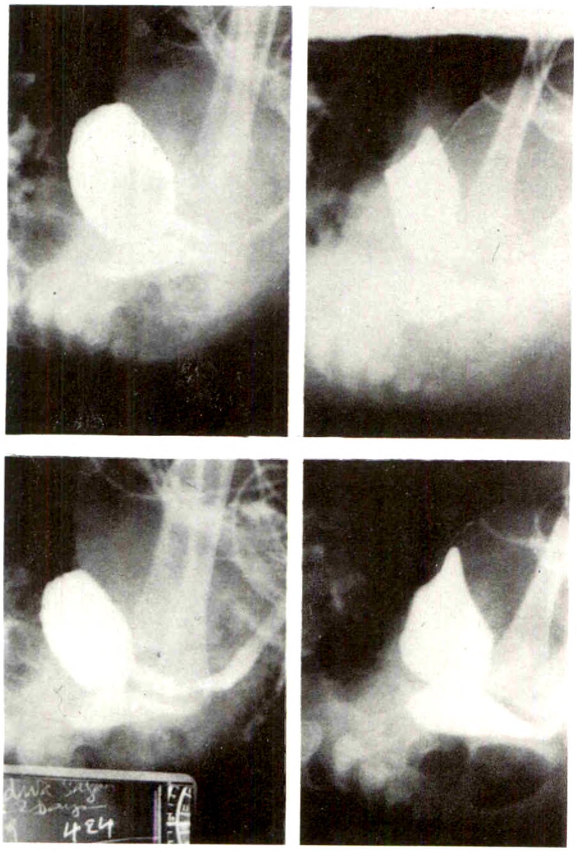

FIGURE 7. Genitography–vaginal hypoplasia and obvious communication between vulvovaginal cavity and vertical urethra.

acidosis. Mineralocorticoid therapy was also given and consisted of intramuscularly administered desoxycorticosterone acetate: 1 mg/kg once daily in newborns and 2 to 5 mg once daily in older children. Orally administered fludrocortisone (Florinef) (0.15 mg/m^2 once daily) along with oral salt replacement (2 g/day) was given when there was salt loss.

Surgical treatment consisted of clitoroplasty, which was usually done by "tucking" a portion of the erectile tissue under the symphysis pubis [2–4], and vulvovaginoplasty, which involved initial exteriorization of the vaginal and urethral orifices [5,6]. These procedures are done between 6 and 18 months of age [2-4]. Some authors believe vaginoplasty should be delayed until after the patient is 6 years old to achieve better results [6]; however, confining the number of surgical procedures by doing both clitoroplasty and vaginoplasty at the same time is better psychologically for the patient and family. Conversely, surgery in patients with Type V and male gender identity requires ablation of the ovarian bodies and uterus before puberty to avoid menstruation through the organs [7].

Follow up included clinical, biological, hormonal, and radiological assessments. Clinical parameters included growth velocity, genital examination (clitoromegaly, phallus size), and pubertal development. Bone age maturation was documented every year. Laboratory investigations included monthly monitoring of serum electrolytes and twice-a-year hormonal assays of ACTH, testosterone, and 17 hydroxyprogesterone, and recently, determination of D4 androstanedione and renin plasmatic activity [2,8]

Discussion

Congenital adrenal hyperplasia is a relatively common disorder in Riyadh, in terms of the number of patients (25 patients over three years) seen in our hospital and the several maternity and children's hospitals of Riyadh and environs.

Most of our patients were Saudis and there was a high frequency (76%) of marriages between first-degree cousins.

Neonatal deaths are still too frequent in those families at risk, as shown in our series (12%). Furthermore, the salt-losing syndrome was very frequent in our series compared with that reported in the literature, 80% versus 33 to 75% [9–13]. This emphasizes the need for neonatal screening in the first days of life for infants born into at risk families [11,14,15]. An equally important consideration are the psychological problems which are amplified by the local sociocultural context and related to the severity of the genital ambiguity. A Type III defect was seen in 53.3% and Type IV and V in 13.3%. These figures are comparable to those reported in the literature [2,7]. Seven of 15 patients (46.6%) who were genetically female had a male name when first seen, and the parents were convinced, sometimes with great difficulty, that the patients were female (46XX).

Intrauterine screening in at risk families is important and should consist of 17 hydroxy-progesterone assay and HLA typing in amniotic cells [16–20]. Hydrocortisone therapy should also be instituted in the mother in the hopes that it will prevent the genital ambiguity [21,22]. However, amniocentesis is not easily accepted in our community because of the risks of abortion in up to 5% of the cases.

Despite all these difficulties, a program of genetic counseling and screening should be strongly advised in families at risk, considering that 92% of our cases are secondary to 21 hydroxylase enzyme deficiency, a percentage similar to that reported in the literature [2,7,12]. This program requires prospective and retrospective studies conducted in the different hospitals of the Riyadh region to yield a better understanding of the disease, its incidence, causes, and consequences. Furthermore, surgical repair of the external genitalia needs a specialized pediatric surgical team working in collaboration with the family physician, the pediatrician, and the psychologist. Such a multidisciplinary team does not yet exist in our hospitals.

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PATTERN OF PRIMARY GASTROINTESTINAL TRACT MALIGNANCY AMONG SAUDI NATIONALS: A RETROSPECTIVE STUDY

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تمت مراجعة تقارير التشريح المرضي النسجي من مختبر مستشفى الرياض المركزي وشملت الفترة مابين ١٤٠٤ إلى ١٤٠٦ (١٩٨٤ - ١٩٨٦م)، وذلك لتحديد نمط السرطان الأولى في السبيل المعدي المعوي بين المواطنين السعوديين. بلغ مجموع ما أجري من فحوص التشريح المرضي النسيجي خلال فترة الدراسة ٣٢٩٩٠ فحصًا. تم التعرف على أورام في ٤٦٨٣ حالة (٢, ١٤٪)، منها ١٧٧٢ ورم خبيث (٨, ٣٧٪) و ٢٩١١ ورم حميد (٢, ٦٢٪). كانت الأورام الخبيثة في السبيل المعدي المعوي هي الأكثر تواترا حيث شكلت نسبة ٤, ٢٧٪ من جميع الحالات. وكانت المعدة (٣١٪)، والكبد (٢٠٪)، والمريء (١٩٪) أكثر الأعضاء إصابة. تختلف نسب تواتر الأورام الخبيثة في السبيل المعدي المعوي عن مثيلاتها في البلدان الغربية وذلك على الرغم من تشابه توزعها بالنسبة للعمر والجنس. وتناقش المقالة العوامل السببية المحتملة مع التأكيد على ضرورة إيجاد سجل لحالات الأورام.

The histopathological reports from the central laboratory of Riyadh Central Hospital for between 1404 to 1406H (1984 to 1986) were reviewed retrospectively to determine the pattern of primary cancer of the gastrointestinal tract among Saudi nationals. During the study period, a total of 32,990 histopathological examinations were conducted. Neoplasms were identified in 4683 cases (14.2%); 1772 (37.8%) were malignant and 2911 (62.2%) were benign. Gastrointestinal malignancy was the most frequent and accounted for 27.4% of all cases. The stomach (31%), liver (20%), and esophagus (19%) were the most commonly involved organs. The proportional frequencies of gastrointestinal malignancies differ from those seen in Western countries, although the age and sex distribution are similar. The possible etiological factors are discussed and the need for a cancer registry emphasized.

Cancer of the gastrointestinal tract is among the leading causes of death in various countries around the world [1,2]. Its incidence shows marked geographic differences, suggesting a strong relationship with environmental and/or dietary factors [3-6]. While the incidence of gastric carcinoma is reported to be decreasing in some countries, it continues to be high in others [7,8]. Reports from Saudi Arabia show that gastrointestinal tract cancer is seen fairly frequently in hospitals across the country [9-12]. The purpose of this study was to determine the pattern of primary malignancy of the gastrointestinal tract as observed in Saudi nationals presenting at Riyadh Central Hospital.

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Accepted for publication 18 February 1990.

Material and Methods

All histopathological reports from the central laboratory of Riyadh Central Hospital during 1404 to 1406H (1984 to 1986) were reviewed to identify cases of gastrointestinal cancer in Saudi nationals. Of the total number of reports, 95% came from Riyadh Central Hospital and other Ministry of Health hospitals in the central region and 5% originated from other parts of the Kingdom. Data on the age, sex, and organ involved were extracted for detailed analysis.

Results

There were 32,990 histopathological examinations done during the 3-year study period. Neoplasms were described in 4683 (14.2%). Of these, 2911 (62.2%) were benign and 1772 (37.8%) were malignant. Eighty-nine cases were excluded from analysis because of duplications or incomplete information. Of the remaining 1683, 497 cases (29.5%) were gastrointestinal tract malignancies, and of these, 377 cases occurred in Saudi nationals (75.8%), whose data were further analyzed.

The stomach (31%), liver (20%), and esophagus (19%) were the organs most frequently affected. The male to female ratio was approximately 2 to 1 (Figure 1) for most tumor locations except for tumors of the gallbladder and small and large intestines, which showed a female preponderance. The stomach is the organ most commonly affected by malignancy in both sexes, followed by the liver in males and esophagus in females.

About 75% of the neoplasms occur in patients between 55 and 75 years of age. Table 1 shows the patient age and site of the gastrointestinal tract malignancies. Cancer of the stomach and colon are more common between the ages of 55 to 75 years. In contast, small intestine malignancies are more common between the ages of 35 and 55 years. Hepatocellular carcinoma occurs more frequently between the ages of 45 and 75 years. Table 2 shows the histological types of the gastrointestinal neoplasms. Three cases of lymphoma of the liver were excluded because information was insufficient to determine whether they were primary lymphomas.

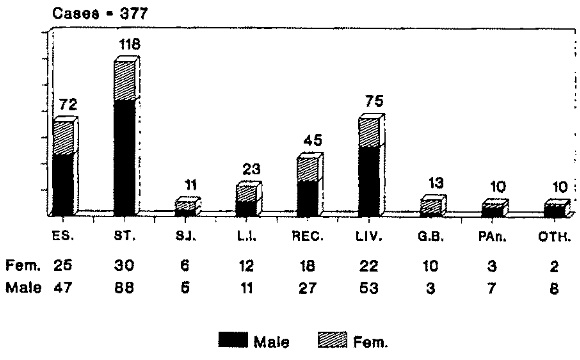

FIGURE 1. Gastrointestinal tract cancer: sex and organ distribution.

Discussion

Our data show that cancer of the stomach is the most frequent gastrointestinal neoplasm. This agrees with observations from Japan but is in contrast with findings reported from Australia, the U.K., and U.S.A., where cancer of the stomach is

TABLE 1. *Cancer of the gastrointestinal tract according to age group and site.*

Site	Age (yr) <1	1–4	5–14	15–24	25–34	35–44	45–54	55–65	66–74	>75	Total
Esophagus	–	–	–	–	–	5	13	21	22	11	72
Stomach	–	–	–	2	3	12	19	32	35	15	118
Small intestine	–	1	–	2	1	3	2	1	–	1	11
Large intestine	–	–	–	–	1	6	8	3	4	1	23
Rectum	–	–	–	1	2	2	13	11	14	2	45
Liver	3	–	1	3	3	4	14	25	17	5	75
Gallbladder	–	–	–	–	–	–	2	4	4	3	13
Pancreas	–	–	–	–	–	1	4	4	1	–	10
Others	1	–	–	–	1	–	5	1	2	–	10
Total	4	1	1	8	11	33	80	102	99	38	377

TABLE 2. *Types of gastrointestinal malignancies among the 377 cases analyzed.*

Organ	No. (%)	Types of malignancy	No.
Esophagus	72 (19.1%)	Squamous cell carcinoma	61
		Adenocarcinoma	11
Stomach	118 (31.3%)	Adenocarcinoma	113
		Lymphoma	2
		Leiomyosarcoma	2
		Carcinoid	1
Liver	75 (19.9%)	Hepatocellular carcinoma	70
		Hepatoblastoma (ages <1 yr)	3
		Cholangiocarcinoma	2
Pancreas	10 (2.7%)	Adenocarcinoma	10
Gallbladder	13 (3.4%)	Adenocarcinoma	13
Small intestine	11 (2.9%)	Adenocarcinoma	4
		Lymphoma	5
		Carcinoid	1
		Kaposi's sarcoma	1
Large intestine	23 (6.1%)	Adenocarcinoma	21
		Lymphoma	2
Rectum	45 (11.9%)	Adenocarcinoma	40
		Squamous cell carcinoma	5
Others	10 (2.7%)	Organ or histological type not specified in the case records	10

the most frequent [1,2]. Unlike other countries, however, the liver is the second most frequent site of cancer. The frequency of carcinoma of the pancreas was relatively low in our series. The esophagus was the third most common site, in agreement with findings from Japan but in disagreement with data reported from other countries. Unlike findings from other countries, colorectal cancer rated fourth in frequency. This is the most common gastrointestinal cancer seen in Australia, the U.K., and U.S.A. while in Japan it is the third most common.

In studies from the Military Hospital and King Faisal Specialist Hospital and Research Centre in Riyadh [10,12], cancer of the liver and esophagus constituted the most common type of gastrointestinal malignancy. The report from the Dhahran Health Centre, like our study, revealed the stomach was the most commonly involved organ [11]. These differences most probably reflect different types of patient populations in these hospitals. Most of these hospitals deal with selected cases of cancer referred for advanced treatment, whereas our cases mostly represent a general hospital population, therefore providing a better picture of the actual pattern of malignancy. Our figures do not, however, represent the true prevalence or incidence of malignancies in the Kingdom. A central tumor registry and population-based studies are required to obtain such data [13]. Our observations need further study to explain the differences observed and perhaps to identify possible causes so that appropriate preventive measures can be adopted. It has been well documented that there is marked variation in the incidence rate of gastrointestinal cancer among different countries and in certain cases even within a country [2,4,6].

The striking geographic variation in the incidence of gastrointestinal cancer emphasizes the importance of local factors such as genetic, dietary, and environmental in the pathogenesis of cancer. In Europe and America, alcohol and tobacco use have been identified as having a part in the etiology of cancer of the esophagus [5]. Alcohol is not a relevant factor in our patients because of the strict enforcement of Islamic law prohibiting alcohol consumption. The use of tobacco was also uncommon in our patients. Poor diet and a deficiency of micronutrients are important in the pathogenesis [5] and could be relevant in our patients because malnutrition has been common in the past. Most of our patients were accustomed to consuming large quantities of hot tea and Arabic coffee containing cardamom. The role of this substance in the etiopathogenesis of gastrointestinal neoplasms is unknown. Prospective studies are required to determine the role of dietary factors in the etiology of carcinoma of the stomach and other gastrointestinal neoplasms.

Acknowledgment

We thank Mr. Buktiar from the Ministry of Health for his assistance in the data collection.

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INCIDENCE OF ROTAVIRAL GASTROENTERITIS AT A REFERRAL CENTRE IN SAUDI ARABIA

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أجريت فحوص استقصائية على التهابات المعدة والأمعاء الناجمة عن حُمة العجَلَة في مستشفى إحالة في المملكة العربية السعودية على مدى أربع سنوات ونصف السنة. ومن بين ١٧٢٩مريضا اشتبه بإصابتهم بالخمج أظهر فحص ٥٤٧ مريضا (٦ , ٣١٪) تفاعلاً إيجابيًا لحُمة العجلة. كان معظم المرضى منومين في المستشفى (٦٥٪) وكانت أعمار ٧ , ٧٥٪ من المرضى دون الاثنى عشر عامًا. وقد عولج داخل المستشفى ٦٣٪ من المصابين دون سن الثانية عشرة البالغ عددهم ٤١٤مريضًا. وكذلك الأمر بالنسبة إلى ٤ , ٤٧٪ من المصابين فوق سن الخامسة والعشرين فقد عولجوا داخل المستشفى لكن حالة ٣ , ٤٠٪ منهم اعتبرت شذوذا في الثوي نظرا لإصابتهم بالأورام أو لإجراء عمليات نقل نقِي العظم لهم.

The incidence of gastroenteritis caused by rotavirus was investigated at a referral hospital in Saudi Arabia over a period of 4.5 years. Of the 1,729 patients with suspected infection, 547 (31.6%) were positive for rotavirus infection. Most were inpatients (65) and 75.7% of the patients were under 12 years of age. Of the 414 positive patients under 12 years of age, 63% were inpatients. Similarly, 74.4% of the 25-year and older group were inpatients. However, 40.3% of them were abnormal hosts because they either harbored neoplasms or had undergone bone marrow transplantation.

Gastroenteritis is a major cause of morbidity and mortality in developing as well as industrialized countries [1,2]. The etiology of the disease can be bacterial, parasitic, or viral. Two major viral agents are implicated; Norwalk virus is primarily associated with outbreaks of gastroenteritis in school, community, or family environments, and affects both children and adults. Rotavirus, on the other hand, has been known to cause both sporadic and epidemic cases of infantile gastroenteritis throughout the world [3]. In general, as much as 50% of the cases of diarrheal disease in hospitalized pediatric patients have been reported to be caused by rotavirus. Four reports have described the incidence of rotavirus infection among infants and children below 3 years of age in Saudi Arabia [4–7]. These studies reported 77 positive samples out of a total of 439 specimens tested. We describe our experience over a period of 4.5 years in 1,729 pediatric and adult patients at King Faisal Specialist Hospital and Research Centre, which is a major referral medical centre in Saudi Arabia.

Material and Methods

Detection of rotavirus in the feces of patients with gastroenteritis was performed by two methods. All diarrheal stool samples were examined by electron microscopy and an enzyme immunoassay test. All formed stool samples were

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Accepted for publication 20 February 1990.

examined by the enzyme immunoassay procedure. Fecal material for electron microscopical examination was prepared by making a 20% stool suspension in 0.01M phosphate-buffered saline at pH 7.6. The suspension was sedimented at 1500 rpm for 10 min in a refrigerated Beckman TJ6 centrifuge. The supernatant was negatively stained with 2% phosphotungstic acid on a 3-mm, 400-mesh Formvar-coated grid and examined by a JOEL 100B transmission electron microscope.

Enzyme immunoassay was performed to detect rotaviral antigens in all fecal specimens with a Rotazyme II kit (Abbott Diagnostics, Irvine, TX), used according to manufacturer's directions. This test employs polystyrene beads that are coated with guinea pig antirotavirus antibodies. Fecal material was prepared by making a 10% suspension in Rotazyme II sample diluent and incubated with the antibody-coated beads for 1 hr at 37°C. After washing three times with distilled water, the beads were incubated with the horseradish peroxidase-antibody conjugate at 37°C for 1 hr. The beads were washed again and 0-phenylenediamine solution containing hydrogen peroxide was added. The tubes were incubated at room temperature for 30 min. Sulfuric acid (1N) was added to the tubes and absorbance was measured on a Quantum II Analyser at 492 nm. Positive and negative controls were provided by the manufacturer and were tested with all batches of patient specimens.

TABLE 1. *Age distribution and incidence of rotavirus infection among inpatients and outpatients.*

	Number		
Age (yr)	Inpatients	Outpatients	Total
<3	203	109	312
3–12	58	44	102
13–24	35	16	51
>24	61	21	82
Total	357 (65%)	190 (35%)	547 (100%)

TABLE 2. *Distribution of rotavirus infection among inpatients in the hospital.*

	Age group/number of patients (%)			
Ward	<3	3–12	13–24	>24
Pediatrics	101 (32.4)	38 (37.3)	N/A	N/A
Oncology/bone marrow transplant	42 (13.5)	9 (8.8)	21 (41.2)	33 (40.2)
General surgery	28 (9.0)	21 (20.6)	6 (11.8)	12 (14.6)
Maternity/obstetrics and gynecology	N/A	N/A	9 (17.6)	8 (9.8)
Miscellaneous	141 (45.2)	34 (33.3)	15 (29.4)	29 (35.4)
Total	312	102	51	82

Results

Stool specimens from 1,729 patients with gastroenteritis at King Faisal Specialist Hospital and Research Centre were tested for rotavirus infection over a period of 4.5 years (January 1985 to August 1989). The hospital is a 513-bed facility in Riyadh that serves a large volume of outpatients and constitutes a major referral centre for the Kingdom. During the period of study, 62,921 patients were admitted to the hospital and 1,502,216 patients were seen in the outpatient clinics. Of the specimens processed from 1,729 patients, 547 (31.6%) yielded positive results. The incidence of rotavirus infection in male patients was slightly higher (57.2%) than that in females. More than half of the patients (57%) were under 3 years of age (Table 1). Although symptomatic gastroenteritis due to rotavirus is infrequent among adults, 26.9% of the inpatients in this study were 13 years or older.

Most rotavirus-positive cases were found in the inpatient population (65%), even though the ratio of outpatients to inpatients was 20:1. The incidence of the virus infection among outpatients and inpatients in various age groups is also shown in Table 1. In almost every age category, twice as many inpatients as outpatients were positive for infection, with 74.4% of the patients in the 25-year or older group being hospitalized.

Most inpatients were being treated in three specialty wards. The highest concentration of young patients (12 years or younger) was in pediatric wards (Table 2). Of the 13 years and older group, 72.6% were from oncology and organ transplant services. Virtually all of these patients were immunosuppressed and on cytotoxic or antimicrobial drugs. No seasonal pattern of rotaviral infectivity was observed, though a high number of cases was recorded not only in

April and June but also in November and December.

Discussion

Acute viral gastroenteritis is a common illness throughout the world. Rotavirus was first implicated as one of the causative agents in 1973 by Bishop et al [8]. They identified rotavirus particles in epithelial cells of duodenal mucosa from six of nine infants with acute nonbacterial gastroenteritis. Since then, the role of rotaviruses as one of the important causes of gastroenteritis has been established throughout the world. In developed countries, rotavirus was found to be the most common enteropathogen, accounting for 42 to 96% of such infections in infants and children with diarrhea and dehydration [7,9–11]. In the United States, the gastroenteritis agent considered a high priority for vaccine development is rotavirus [12]. The incidence in developing countries, on the other hand, is low (3–24%) with most infections caused by bacterial or parasitic agents [13–16]. However, Bartlett et al [17] estimated that rotaviruses are responsible for more than a million deaths in young children each year in the developing world. The incidence of rotavirus infection in pediatric Saudi patients has been described [4–7]. Although adults are less likely to become infected [18,19], infections do occur [20,21]. In the present series, 24.3% of the patients were 13 years or older, and to our knowledge, this is the first report of adult rotavirus gastroenteritis in a Saudi population. In spite of a high outpatient-to-inpatient ratio at the hospital, more inpatients than outpatients were infected with rotavirus.

Immunosuppression, the administration of cytotoxic drugs, and prolonged antibacterial therapy are well-known conditions that can make patients susceptible to opportunistic viral infections such as cytomegalovirus, herpes simplex virus, varicella zoster virus, and Epstein-Barr virus. Cases of chronic rotavirus infection in immunodeficient children and in geriatric patients with malignancies, hemiparesis, pneumonia, pulmonary embolism, senile dementia, and other underlying multiple problems have been reported [22,23]. Fifteen percent of the children 2-years-old and younger and almost 78% of 13-years-old and older inpatients at our hospital were from oncology and bone marrow and tissue transplant services. Thus, rotavirus seems to be emerging as an opportunistic pathogen in debilitated and immunocompromised patients.

Acknowledgments

We wish to thank the staff of the Diagnostic Virology and Electron Microscopy Units for their technical assistance. We also thank Delia Bonifacio and Ofelia Frias for secretarial assistance.

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THE EFFECT OF FASTING IN RAMADAN ON HEMOSTATIC VARIABLES

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جرى قياس معالم إرقائية في الصباح وبعد الظهر خلال شهر رمضان المبارك على ٣٣ متطوعا، ثم أعيد قياسها في يوم عادي ليس فيه صوم. لم تكن هناك تقلّبات نهارية ذات مغزى في معالم الإرقاء في البلازما سواء في رمضان أو في أيام الفطر. كما لم يكن هناك فرق في استجابات تكدّس الصفيحات صباحا أو بعد الظهر بين فترة الصوم في رمضان وأيام الفطر.

إلا أن استجابات التكدّس لثاني فسفات الأدينوزين، ADP (٢ميكروميتر/ل)، والأدرينالين، والكُلّاجين، وحمض الأراكيدونيك أظهرت انخفاضا خلال رمضان بالمقارنة مع أيام الفطر. يستنتج من هذا أن الإجهاد الذي يلقاه الصائم في رمضان، حسبما يتضح من استجابات تكدّس الصفيحات، هو أقل من الإجهاد الذي يلقاه المرء في أيام الفطر.

Hemostatic measurements were performed in 33 volunteers in the morning and afternoon in one day during the Muslim fasting month of Ramadan, and were then repeated on an ordinary nonfasting day. There were no significant diurnal fluctuations in plasmatic hemostatic parameters either in Ramadan or on a nonfasting day. There was no difference in the morning and afternoon platelet aggregation responses between Ramadan and the nonfasting period. However, aggregation responses to ADP (2 μM/L), adrenaline, collagen, and arachidonic acid were diminished during Ramadan as compared to the nonfasting day. It is concluded that the stress encountered during the Ramadan fast, as depicted in the platelet aggregation responses, is less than that encountered on an ordinary nonfasting day.

The fasting month of Ramadan is the ninth lunar month of the Muslim calendar. It is during this time when all Muslims are obliged to observe a dawn to sunset fast, but may consume any food and drink from sunset to dawn. Previous studies on the physiological responses to Ramadan fasting have documented biochemical [1–7], hematological [3,6,8], and hormonal [4] changes, but no studies have been done to investigate the responses of the hemostatic system. The total fast during an ordinary working day is stressful, and it is well established that a wide variety of stressful stimuli produce measurable effects on platelet function, coagulation, and fibrinolysis [9].

We report the results of measurements of a variety of hemostatic variables, including platelet aggregation, in healthy volunteers observing the Ramadan fast. The same measurements were repeated in an ordinary working day. As far as we know, no similar study has been done before.

Material and Methods

A total of 33 volunteers (30 males, 3 females) were studied (mean age, 32 ± 4.98 yr SD; mean weight, 69.9 ± 7.98 kg SD). They were members of the academic, technical, or clinical staff, or students at the College of Medicine, as well as members of the general public. Only three subjects smoked an average of less than 10 cigarettes per day; the rest were nonsmokers.

Ramadan blood samples were obtained at 9:00 A.M. and 3:00 P.M., five and ten hours after the last intake of food or drink during a working day in

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Accepted for publication 3 March 1990.

the third week of Ramadan (9:00 A.M. and 3:00 P.M. are the start and end of the working day during Ramadan). The same subjects were studied again during a nonfasting day (working hours, 7:30 A.M. to 4:30 P.M.), and blood samples were drawn at the same time of day as during the fasting period. The 7:30 A.M. sample was taken after the subject had ingested a cup of tea and biscuits but no fatty food; the 4:30 P.M. samples were collected approximately 2 to 3 hours after an ordinary lunch had been eaten. Blood samples were collected from an antecubital vein with the minimum of venous stasis and added to sodium citrate (0.11 M) in a vacutainer plastic tube (Sarstedt, West Germany) to yield a blood:citrate ratio of 9:1. Blood for platelet counts was also collected directly into EDTA tubes (Sarstedt, West Germany).

The following tests were performed: prothrombin time (PT) and partial thromboplastin time (Ortho-Diagnostic Reagents); thrombin time (Parke Davis Topical Thrombin); reptilase time (Pentapharm, Switzerland); plasma fibrinogen (turbometic method of Ellis and Stransky [10]); antithrombin III by the chromogenic assay [11] using substrate S2238 (Coatest kits; Kabi, Sweden); platelet count using a thrombocounter (Coulter Electronics); FVIII:C (chromogenic assay [12]) employing Coatest Kits (Kabi, Sweden), the von Willebrand factor–ristocetin cofactor (vWF:RiCof) according to the method of Macfarlane et al [13], factors X, V, and VII [14]; plasminogen and alpha-2-antiplasmin by the chromogenic assay [15] (Berichrom Kits; Behring, West Germany).

Platelet aggregation was performed in response to ADP (20, 2.0, 1.0, and 0.5 μM/L), collagen (0.19 g/L), adrenaline (100 mmol/L), arachidonic acid (1.64 mmol/L), and ristocetin (150, 120, and 100 mg/dl), as detailed recently [16]. All these concentrations of the aggregating agents were final concentrations, obtained by adding 20 μl of agonist to 180 μl of platelet-rich plasma, and the result was recorded on an aggregometer (Aggregation Profiler-PAP4; Bio/Data Corp., USA).

Since the data obtained demonstrated normal distribution, the results were expressed as the mean ± standard deviation. The unpaired Student's t test was used to examine the significance between groups of data.

Results

A summary of the results is shown in Tables 1 and 2 and results are given as the mean and standard deviation for the various hemostatic variables.

Coagulation Tests

There was no obvious difference in measurements of all the plasmatic coagulation variables when comparing the morning and afternoon measurements, whether in Ramadan or the ordinary nonfasting day (Table 1). A slight reduction in the platelet count was noted when the morning and afternoon values were compared for the nonfasting day but the difference was not statistically significant. Neither age, weight, nor sex had any significant effect in these measurements. Antithrombin III was the only parameter that showed significant decreases in Ramadan ($P < 0.02$) when compared to the levels recorded for the nonfasting day, but both measurements were within the normal range of 80 to 120% for the local population. Similarly, antithrombin III levels were also significantly lower in the afternoon during Ramadan when compared to those obtained on the nonfasting day ($P < 0.005$).

In assessing platelet aggregation, no obvious differences were noted between the morning and afternoon measurements, both for Ramadan and the nonfasting days (Table 2). At the lowest dose of ADP (0.5 μM/L), the afternoon aggregation response in Ramadan was lower than the morning response, but this difference was not statistically significant.

There was significant reduction in the aggregation responses to ADP (2.0 μM/L) ($P < 0.005$), collagen ($P < 0.02$), adrenaline ($P < 0.005$), and arachidonic acid ($P < 0.01$) in the Ramadan morning responses when compared with the nonfasting morning responses. However, the responses to the lower doses of ristocetin (120 and 100 mg/dl) showed an opposite trend with higher responses during Ramadan ($P < 0.05$ and 0.005, respectively) than on the nonfasting day.

The variations noted for the morning measurements were confirmed in the afternoon responses to ADP (2.0 μM/L) ($P < 0.05$), collagen ($P < 0.01$), and adrenaline ($P < 0.01$). Similarly, low-dose ristocetin (120 and 200 mg/dl) produced higher responses during the Ramadan afternoon

TABLE 1. *Morning and afternoon measurements of coagulation parameters during Ramadan compared to control values in a nonfasting day.*

Variables	Fasting (Ramadan) (mean ± SD) (No.) Morning	Fasting (Ramadan) (mean ± SD) (No.) Afternoon	Nonfasting (mean ± SD) (No.) Morning	Nonfasting (mean ± SD) (No.) Afternoon
PT (sec)	11.7 ± 0.6 (33)	11.5 ± 0.8 (33)	11.8 ± 0.5 (18)	11.9 ± 0.5 (18)
PTT (sec)	25.8 ± 2.8 (33)	25.5 ± 2.5 (33)	26.5 ± 2.1 (18)	26.1 ± 2.2 (18)
TT (sec)	14.3 ± 3.5 (31)	14.2 ± 3.6 (31)	14.1 ± 1.9 (14)	14.3 ± 1.7 (18)
RT (sec)	12.7 ± 0.9 (31)	12.2 ± 0.9 (32)	11.3 ± 0.8 (18)	11.5 ± 0.8 (18)
Fibrinogen (g/L)	2.68± 0.95 (31)	2.76± 0.84 (31)	3.0 ± 0.88 (15)	2.75± 0.59 (15)
AT III (%)	94.7 ± 8.9 (28)	95.9 ±12.6 (28)	106.0±13.9 (15)	111.5± 9.6 (15)
Platelet count ($\times 10^9$/L)	233.2±57.8 (32)	237.1±59.1 (32)	272.3±59.3 (16)	261.7±54.1 (16)
FVIII:RiCoF (%)	72.7 ±35.1 (32)	80.4 ±39.0 (32)	85.2 ±65.1 (18)	64.3 ±44.9 (18)
FVIII:C (%)	110.8±40.4 (33)	105.6±34.9 (33)	99.3 ±21.1 (18)	102.1±16.6 (18)
Plasminogen (%)	81.9 ± 9.1 (33)	81.9 ± 7.7 (33)	79.6 ±11.1 (18)	76.6 ±10.8 (18)
α_2-Antiplasmin	97.0 ±14.4 (31)	96.3 ±12.1 (32)	107.5±19.0 (18)	102.6±11.8 (18)
FX (%)	108.3±21.7 (31)	103.9±16.6 (32)	99.3 ±21.1 (18)	102.6±16.6 (18)
FV (%)	109.0±13.8 (13)	113.4±22.2 (13)	–	–
FVII (%)	99.7 ±20.6 (13)	96.7 ±21.6 (13)	–	–

– = not done; PT = prothrombin time; PTT = partial thromboplastin time; TT = thrombin time; RT = reptilase time; AT III = antithrombin III; FVIII, FX and FV = Factors VIII, X and V, respectively; R:CoF = ristocetin co-factor.

TABLE 2. *Morning and afternoon measurements of platelet aggregation (expressed as slope and maximum aggregation) during Ramadan as compared to control values on a nonfasting day.*

	Fasting (Ramadan)				Nonfasting			
	Morning		Afternoon		Morning		Afternoon	
	Slope	MA%	Slope	MA%	Slope	MA%	Slope	MA%
ADP 2 (μM/L)	39.4 ± 16.3 (33)	60.2 ± 17.3 (33)	36.1 ± 10.2 (33)	54.6 ± 24.1 (33)	47.3 ± 10.4 (18)	76.9 ± 11.1 (18)††	48.5 ± 12.0 (18)†	77.3 ± 19.0 (18)†
ADP 1 (μM/L)	28.6 ± 11.8 (28)	30.9 ± 19.8 (28)	25.6 ± 10.0 (24)	25.4 ± 22.2 (24)	25.6 ± 13.8 (18)	30.0 ± 28.9 (18)	23.3 ± 12.8 (16)	32.4 ± 27.6 (16)
ADP 0.5 (μM/L)	27.4 ± 11.1 (8)	40.6 ± 20.7 (8)	18.3 ± 5.5 (8)	18.2 ± 10.4 (8)	20.0 ± 9.2 (6)	39.2 ± 36.3 (6)	18.5 ± 8.4 (4)	33.5 ± 28.3 (4)
Collagen (0.19 g/L)	45.4 ± 11.9 (26)	66.89 ± 9.7 (26)	46.6 ± 11.0 (26)	67.9 ± 10.9 (26)	54.71 ± 9.4 (17)**	72.4 ± 9.5 (17)	56.71 ± 9.5 (17)*	72.35± 7.7 (17)*
Adrenaline (100 mmol/L)	14.7 ± 10.7 (33)	63.2 ± 20.6 (33)	13.9 ± 11.5 (33)	59.3 ± 28.2 (33)	26.4 ± 9.1 (18)††	70.9 ± 17.1 (18)	24.5 ± 10.0 (16)*	67.2 ± 24.0 (16)
Arachidonic acid (1.64 mmol/L)	33.8 ± 18.7 (26)	63.4 ± 27.2 (26)	38.4 ± 17.1 (26)	70.5 ± 28.0 (26)	48.2 ± 8.4 (17)†	78.6 ± 6.0 (17)*	45.5 ± 9.1 (18)	76.3 ± 8.1 (18)
Ristocetin (250 mg/dl)	40.7 ± 18.3 (32)	80.5 ± 12.4 (32)	43.4 ± 14.3 (32)	80.9 ± 14.1 (32)	46.9 ± 14.3 (17)	79.5 ± 16.9 (17)	47.6 ± 12.1 (16)	86.1 ± 8.1 (16)
Ristocetin (120 mg/dl)	26.1 ± 14.9 (31)	70.2 ± 23.6 (31)*	27.1 ± 15.8 (31)	69.7 ± 25.5 (31)†	26.3 ± 13.7 (16)	46.9 ± 31.6 (16)	26.1 ± 10.5 (16)	51.2 ± 31.9 (16)
Ristocetin (100 mg/dl)	22.1 ± 19.7 (23)†	57.9 ± 33.9 (23)††	20.8 ± 16.4 (23)†	51.3 ± 37.1 (23)††	10.0 ± 5.9 (9)	13.5 ± 7.6 (9)	9.0 ± 7.5 (11)	9.64± 7.5 (11)

P values: * = < 0.01; ** = < 0.02; † = < 0.05; †† = < 0.005. *P* values represent the levels of significance of the differences between respective morning and afternoon measurements in fasting (Ramadan) versus nonfasting days.

MA% = maximal aggregation.

NB: Values are expressed as the mean ± SD with the number of subjects used for measurements in parentheses.

when compared with the nonfasting afternoon ($P < 0.05$ and < 0.005, respectively). No significant differences were noted with respect to arachidonic acid and high-dose ristocetin (150 mg/dl) responses.

Discussion

In this study we observed no significant diurnal variations in the levels of plasmatic hemostatic parameters for either Ramadan or ordinary nonfasting days. However, platelet aggregation responses were diminished in Ramadan when compared with those observed on nonfasting days.

Findings from a previous study have suggested that the incidence of renal colic and angina pectoris increases noticeably during Ramadan, especially when it falls in the hot summer season [1]. This raises the question whether the Ramadan fast induces a hypercoagulable prothrombotic state similar to that associated with other forms of stress [9]. Our results indicate the opposite, as we observed a lower platelet aggegability in Ramadan than during the nonfasting day. The more enhanced aggregation response on the nonfasting day cannot be related to cigarette smoking, as only three of the 31 subjects were light smokers and they were instructed to abstain from smoking at least two hours before blood sampling. It is known that cigarette smoking provokes acute platelet activation that lasts for 30 to 60 minutes after each cigarette [17].

Ramadan is the most holy month in the Islamic calendar, when Muslims are expected to abstain not only from food and drink but also from smoking, sexual contact, and heated arguments or discussions. When observing the fast, Muslims are also obliged to perform many religious rituals which makes peace of mind a salient feature of Ramadan. As a consequence, Ramadan puts much less mental strain on daily life than what is normally encountered in an ordinary nonfasting day. A similar conclusion was reported previously [8] in a study that examined the eosinophil count as an index of stress and emotional imbalance.

The lack of significant fluctuations in plasmatic coagulation parameters both during Ramadan and in the nonfasting day is not unexpected, as it is known that the diurnal variations in these variables is minimal [18].

Previous studies have reported elevated levels of cholesterol and triglycerides during Ramadan [1,3,4–6]. It is also known that the increase in plasma lipid levels as a result of prolonged (72 hours) fasting is associated with enhanced platelet aggregation and thrombotic tendency [19,20]. The Ramadan fast lasts for approximately 15 hours and the reported increase in plasma lipid levels does not reach the pathological levels associated with abnormalities in platelet function [20–23].

We found no reason that would account for the more enhanced aggregation responses to ristocetin seen during Ramadan when compared with those seen in the nonfasting day. Ristocetin interacts quantitatively with vWF:ricofactor and a platelet receptor (GPIb) to cause platelets to aggregate [24]. In this study, ricofactor activity (Table 2) is comparable in both Ramadan and the nonfasting measurements. This excludes the possibility that ricofactor may be responsible for these different responses. The ristocetin responses, therefore, remain unexplained.

It should be emphasized, however, that the subjects in this study were office workers who were not exposed to the high (above 40°C) temperatures of the Arabian summer, and therefore they did not suffer from any degree of dehydration. Our earlier study [2] and those of others [3,6] have shown that the hematocrit in such subjects was hardly affected by the Ramadan fast. Therefore, the results might have been different if the subjects' work had entailed excessive exposure to the sun (e.g., workers on construction sites). However, such subjects are always difficult to obtain blood samples from in Ramadan because of the unfounded belief that donation of blood spoils the fast.

This study showed that the Ramadan fast does not influence the plasmatic coagulation parameters. However, the responsiveness of platelets to a variety of agonists is less in Ramadan than that on ordinary nonfasting days. Thus the Ramadan fast puts less strain on the hemostatic system than what is normally encountered in an ordinary working day. As a corollary of these observations, routine testing of the hemostatic system in patients can be undertaken in Ramadan with no concern about any significant influence of the fast on the measured levels, as is the case with some biochemical [1–7] and hematological [3,6,8] parameters. Our study also strongly supports the recent findings of Saour et al [25] that Ramadan fasting has no adverse effect on the efficacy and safety of long-term oral anticoagulation.

Acknowledgments

We thanks Messrs. G. Mackay and M. A. Hamid and Mrs. M. J. Dalziel-Jones for their excellent technical assistance; Dr. A. Lambourne for statistical help; and Mrs. F. Chatila for typing the manuscript. This work was supported by Grant No. AR-5-99 from the King Abdul Aziz City for Science and Technology.

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THE MORPHOLOGICAL SPECTRUM OF TUMORS OF ADIPOSE TISSUE: A PATHOLOGICAL ANALYSIS OF 685 TUMORS

Mohamed B. Satti, MRCPath(Lond)

سجل قسم الباثولوجيا بمستشفى الملك فهد الجامعي ، بالخبر، ١٠٩٣ حالة من الأورام منشؤها في الأنسجة الرخوة على مدى سبع سنوات. ومن تلك الحالات، أجري تحليل باثولوجي نسيجي لخمسة وثمانين وستمائة ورم تعود نشأتها إلى النسيج الشحمي وتم استئصالها من ٦٤٠ مريضاً. ومن الأورام المتعددة الخمسة والأربعين وجدنا ٣١ورمًا وعائياً دهنياً و١٤ ورمًا شحمياً. أما من إجمالي الأورام فقد كان هناك ٥٧٩ ورما شحميا تم استئصالها من ٥٦٥ مريضا، و٨٩ ورما وعائيا دهنيا تم استئصالها من ٥٨ مريضا، وثلاثة أورام شحمية ذات الخلايا المغزلية، وأربعة أورام شحمية عديدة الأشكال، وورمين من النوع الشحمي النخاعي، وورمين من النوع الشحمي العضلي الوعائي، وستة أغران شحمية. حدثت معظم أورام النسيج الشحمي في الذكور بنسبة ٣ : ١ وأصابت في الغالب ذكورا تتراوح أعمارهم بين ١٦ و ٦٠ عاما (متوسط العمر الاجمالي ٣٧ عامًا). كانت منطقة الجذع أكثر المواقع إصابة. تتناول هذه الدراسة بالشرح والتحليل الأنماط الثانوية النسيجية وعلاقتها بالمعالم السريرية.

Over a seven-year period, 1093 cases of tumors of soft-tissue origin were recorded by the Pathology Department of King Fahd Hospital of the University, Al-Khobar. Of these, detailed histopathological analysis was performed on 685 tumors of adipose-tissue origin removed from 640 patients. Of the 45 multiple tumors, 31 were angiolipomas and 14 were lipomas. Of the total tumors there were 579 lipomas removed from 565 patients, 89 angiolipomas removed from 58 patients, three spindle-cell lipomas, four pleomorphic lipomas, two myelolipomas, two angiomyolipomas, and six liposarcomas. The majority of adipose-tissue tumors occurred in males, for a ratio of 3:1, and dominantly affected patients in the age range 16 to 60 years (overall mean age, 37 years). The most common site affected was the trunk. The histological subtypes as correlated to their clinical parameters are presented and discussed.

Tumors of adipose-tissue origin (TATO) are the most common tumors with a soft-tissue origin (TSTO). Lipomas in particular are considered the most common neoplasm of mesenchymal origin [1]. Included within the lipoma group are less common though interesting variants—namely angiolipoma, intramuscular lipoma, and the recently categorized spindle-cell and pleomorphic lipomas [2-4]. Histological recognition of these variant entities is mandatory, as they can easily be misdiagnosed as liposarcomas [5].

Liposarcoma, likewise, next to malignant fibrous histiocytoma, is the most common sarcoma seen in adults [1], with a 16 to 18% incidence [6,7]. The remarkable variability in the histological picture of liposarcoma, ranging from well-differentiated lipoma-like to poorly differentiated pleomorphic neoplasm may be a factor in the misdiagnosis of this neoplasm. The degree of differentiation of these tumors, however, is currently taken as the

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Accepted for publication 27 February 1990.

most reliable criterion in predicting the clinical behavior following excision [1,6,8–10].

Because of the relatively frequent occurrence of TATO, I opted to study such tumors encountered over a seven-year period, in order to determine their morphological spectrum and their relative frequency among TSTO, comparing these results with those reported in the literature.

Material and Methods

The material was obtained from the records of the Pathology Department of King Fahd Hospital of the University, Al-Khobar, during 1983 to 1989, inclusive. Paraffin blocks and histological sections pertinent to all cases labeled as soft-tissue tumors were retrieved. Histopathological screening was performed on hematoxylin-eosin (H&E)-stained sections to classify these tumors and particularly to segregate those of adipose tissue origin. The latter group were further evaluated histologically and classified using standard histological criteria [1]. When necessary, further sections were cut from the paraffin blocks and stained using H&E, phosphotungstic acid–hematoxylin, and Gordon and Sweet reticulin stains. Phosphotungstic acid–hematoxylin was used to demonstrate cross striations in suspected rhabdomyosarcomas. Finally, the following information was extracted from patient records: age, sex, nationality, site, number of tumors, and size in centimeters. The histological findings combined with the clinical information were studied and analyzed.

Results

The number of all TSTO encountered in the seven-year period was 1093, and this constituted 51% of all benign and malignant neoplasms diagnosed in the laboratory during the same period (2120 tumors). Of the 1093 TSTO, there were 685 TATO, accounting for 62.7% of TSTO and 32% of all neoplasms diagnosed during the same period. The remaining TSTO are listed in Table 1.

The 685 TATO were removed from 640 patients, the result of multiplicity of some tumors. These additional tumors were more commonly angiolipomas and occurred in 31 patients. Multiple lipomas occurred in 14 patients. The histological breakdown of these tumors is shown in Table 2. The tumors occurred with almost equal frequency in both Saudis and non-Saudis.

Among the 640 patients with TATO, 480 were males (M:F = 3:1). There was no female dominance noted for any of the histological subtypes. Moreover five of the seven patients with spindle-cell and pleomorphic lipomas were male. The mean age of all patients was 37 years (range, 2–91

TABLE 1. *Morphological spectrum of 1093 cases of TSTO.*

Type	No.(%)
TATO	685 (62.7)
Hemangioma	115 (10.5)
Leiomyoma	93 (8.5)
Neurofibroma	61 (5.6)
GCTTS	34 (3.1)
Schwannoma	32 (2.9)
Leiomyosarcoma	13 (1.2)
DFP	11 (1.0)
Myxoma	2 (0.2)
MFH	7 (0.6)
Rhabdomyosarcoma	7 (0.6)
Kaposi's sarcoma	5 (0.5)
Fibromatosis	13 (1.2)
Synovial sarcoma	3 (0.3)
Hemangiosarcoma	1 (0.1)
Hemangiopericytoma	3 (0.4)
Fibrosarcoma	4 (0.4)
JAF	1 (0.1)
ASPS	2 (0.2)
Osteosarcoma (EO)	1 (0.1)

TATO = tumors of adipose-tissue origin; GCTTS = giant-cell tumor of tendon sheath; DFP = dermatofibrosarcoma protuberans; MFH = malignant fibrous histiocytoma; ASPS = alveolar soft part sarcoma; JAF = juvenile aponeurotic fibroma; EO = extraosseous; TSTO = tumors with a soft-tissue origin.

TABLE 2. *Histological classification of 685 TATO occurring in 640 patients.*

Tumor type	Single	Multiple	No.(%)
Lipoma	565	14	579 (84.5)
Angiolipoma	58	31	89 (13.0)
Pleomorphic lipoma	4	–	4 (0.6)
Spindle-cell lipoma	3	–	3 (0.4)
Myelolipoma	2	–	2 (0.3)
Angiomyolipoma	2	–	2 (0.3)
Liposarcoma	6	–	6 (0.9)
Total	640	45	685

TATO = tumors of adipose tissue origin.

years). The respective mean age for those with lipoma and angiolipoma was 36 and 33 years, respectively. Of all patients, only 13 were younger than 16 years and 23 were older than 60. Of the patients with angiolipoma, only one was younger than 16 and none were older than 60. All six patients with liposarcoma were 40 years or over. Mean age for the seven patients with spindlecell and pleomorphic lipomas was 48 years (range, 45–55 years).

Of the 579 lipomas, 345 were located on the trunk, 228 on the upper and lower limbs, and six in the spermatic cord. Seventy of the 89 angiolipomas, however, were located subcutaneously on the upper limbs and trunk. Of the three spindle-cell lipomas, one was located on the forehead, one on the posterior neck, and one on the dorsal aspect of the wrist joint. Three of the four pleomorphic lipomas were located in the interscapular area and the fourth was located in the left groin. Both angiomyolipomas were of renal origin and were diagnosed at nephrectomy. The myelolipomas were located around the left adrenal gland and were removed using the same surgical technique as used for lipomas. Three of the six liposarcomas were located on the thigh and three in the retroperitoneum.

Of all lipomas, only 36 were greater than 10 cm in diameter. Of the angiolipomas, however, only four were more than 5 cm and none was more than 10 cm in diameter. All seven spindle-cell and pleomorphic lipomas were less than 10 cm in diameter. Both angiomyolipomas were above 10 cm in diameter, yellowish with tan brown areas, and situated in the renal pelvis. All six liposarcomas were more than 15 cm in diameter and contained areas of softening and necrosis. All of the benign lipomatous tumors, including the two angiomyolipomas, were well circumscribed and on gross inspection had a noninvasive appearance.

Histological Evaluation

Examination of paraffin sections revealed no additional information on the common lipomas that had been diagnosed as such on clinical and surgical grounds. Some of the angiolipomas were regarded clinically as hemangiolipomas or hemangiomas. Histological examination of these angiolipomas showed the characteristic appearance of nodules of capillary proliferation in a background of adipocytes (Figure 1). The degree of vascular proliferation varied markedly. An almost constant feature of these lesions was the presence of fibrin thrombi within the capillaries (Figure 2). No atypia was noted and there was no confusion with liposarcoma. Spindle-cell lipomas were more cellular, less vascularized, and had a slight myxoid change. No mitoses or features suggesting malignancy were noted. Conversely, the four cases identified as pleomorphic lipomas all showed pleomorphism and had scattered multinucleated giant cells with characteristic hyperchromatism. Some of these giant cells exhibited the "floret" pattern described by Enzinger [5]. All these cells were set in a background of adipocytes, short collagen fibers, and myxoid areas (Figure 3). Lipoblasts or increased mitoses were not notable features. The diagnostic cellular areas varied markedly in quantity among the four types of tumors. In two, such areas were limited to only a few microscopic foci that could have been missed, had it not been for the opportunity to examine multiple sections.

The two renal angiomyolipomas were characterized histologically by a proliferation of a mixture of adipocytes, smooth muscle fibers, and blood vessels. All three elements were intimately related and mixed. Both myelolipomas were composed of adipocytes mixed with collections of hematopoietic elements—namely megakaryocytes, normoblasts, and myeloid cells.

Of the six liposarcomas, three were myxoid, two were well differentiated, and one was a round-cell variant. Lipoblasts were evident in all tumors (Figure 4). The myxoid variants had the characteristic capillary meshwork separating the myxoid cellular areas. In addition, the round-cell variant had minor foci of myxoid degeneration separating the undifferentiated round cells (Figure 5).

Discussion

Lipomas are the most common benign neoplasms of mesenchymal origin [1], and this is borne out by our observations which revealed that the TSTO encountered by our laboratory constituted 51% of all neoplasms removed during the study period. This agrees with the findings from previous reports that identify TATO as the most common of TSTO [1]. They accounted for 62.7% of TSTO and 32% of all benign and malignant

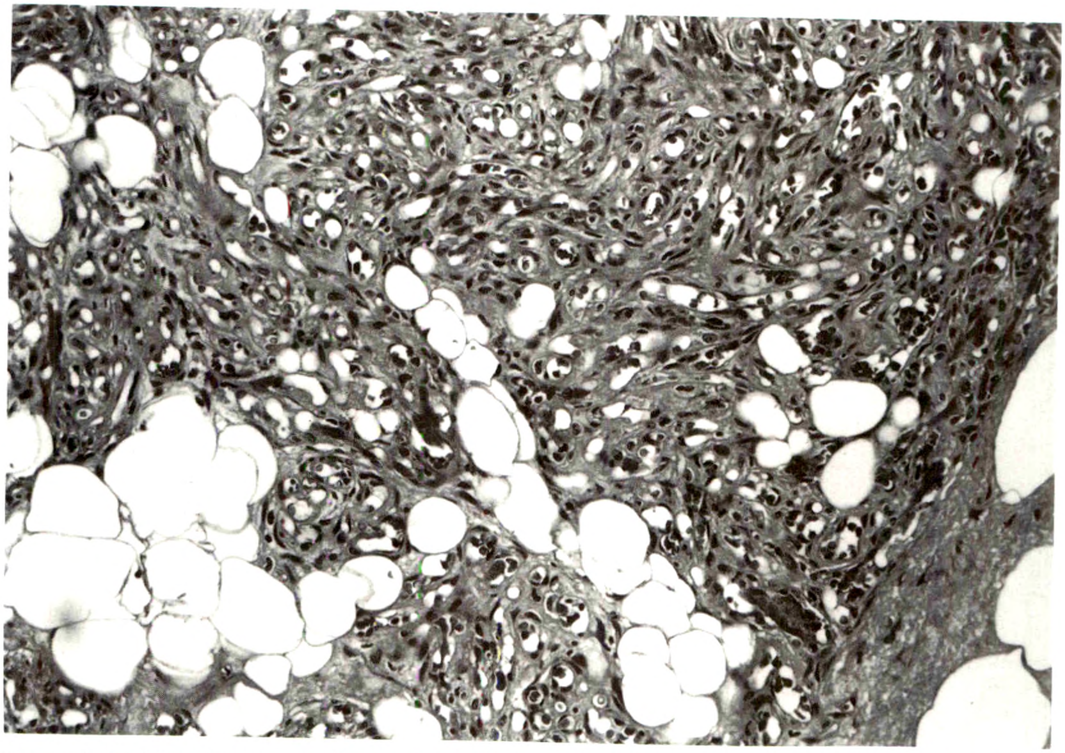

FIGURE 1. Nodules of capillary proliferation in a background of adipocytes in an angiolipoma. (H&E; original magnification, × 125.)

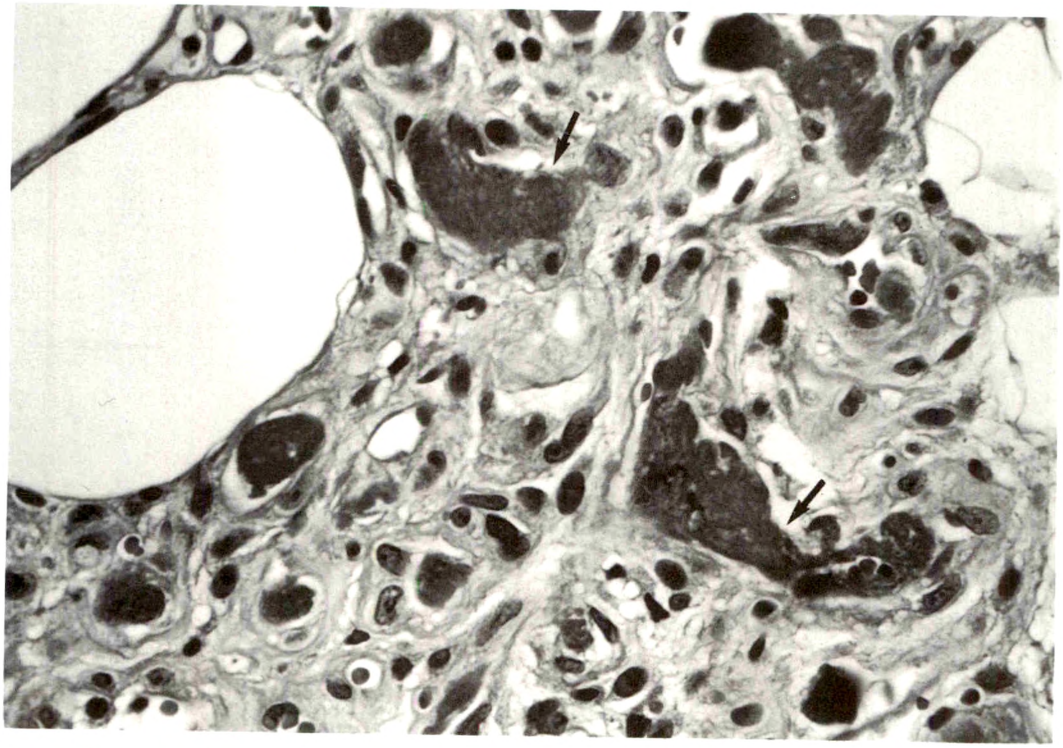

FIGURE 2. Proliferating capillaries containing fibrin thrombi in an angiolipoma *(arrows)*. (H&E; original magnification, × 325.)

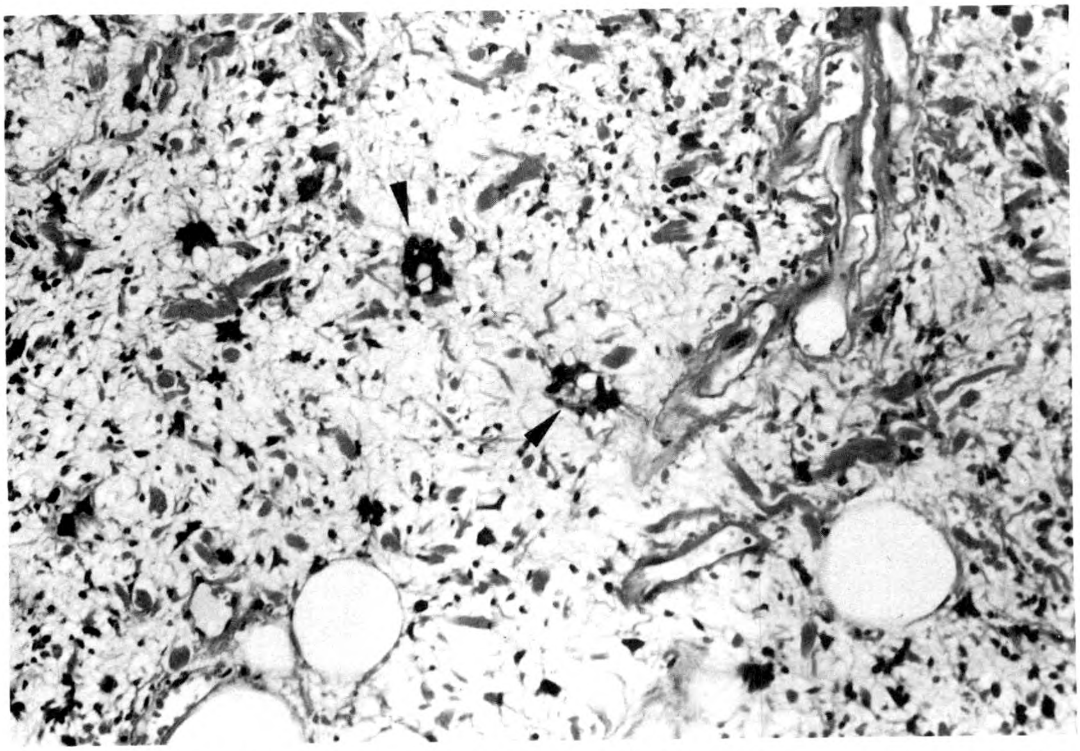

FIGURE 3. Pleomorphic lipoma. Multinucleated "floret" giant cells *(arrowhead)* with hyperchromatic nuclei in a background of adipocytes, short collagen fibers, and myxoid areas. (H&E; original magnification, × 125.)

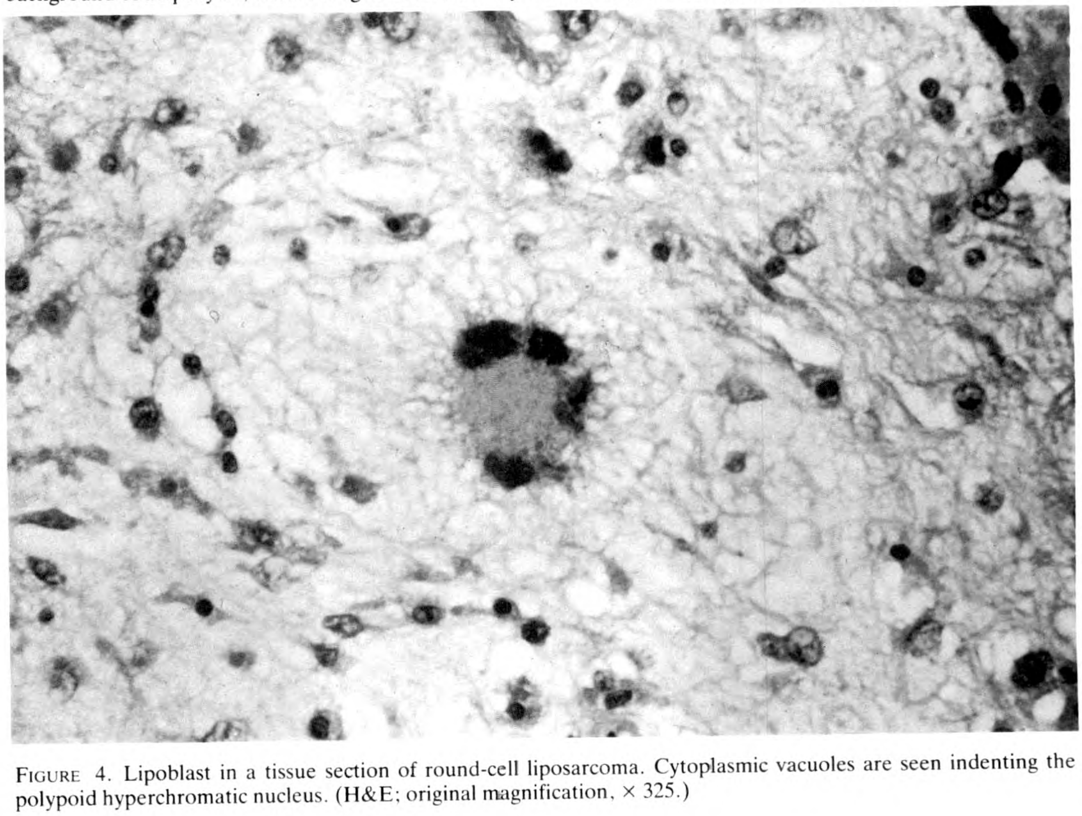

FIGURE 4. Lipoblast in a tissue section of round-cell liposarcoma. Cytoplasmic vacuoles are seen indenting the polypoid hyperchromatic nucleus. (H&E; original magnification, × 325.)

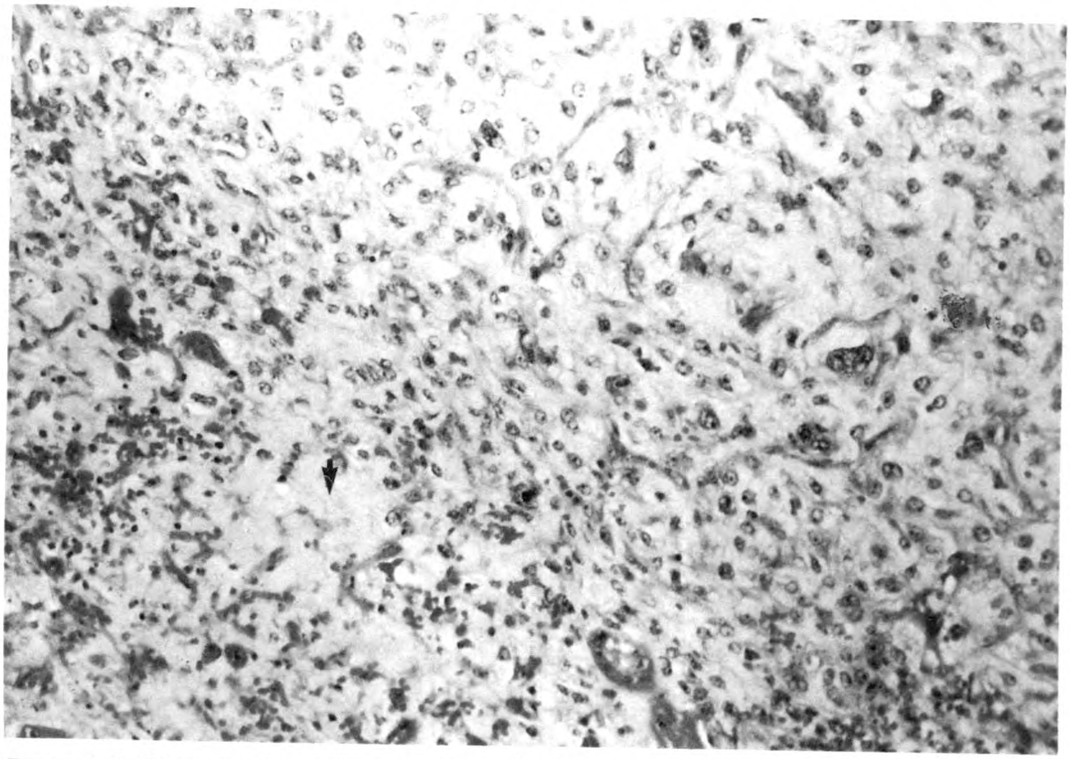

FIGURE 5. Cellular tumor formed of round undifferentiated cells, few obliterated vessels, and scattered lipoblasts. Focal myxoid degeneration is seen *(arrow)*. (H&E; original magnification, × 125.)

neoplasms examined during the study period. Of all the histological subtypes of TATO, ordinary lipomas headed the list (84.5%), as expected, followed by angiolipomas (13%). The remaining subtypes, including liposarcoma, constituted only 2.5%. These results agree with those from the previous studies [2-4]. Among all 57 soft-tissue sarcomas reviewed (see Table 1), there were six liposarcomas, amounting to 10.5%. This figure is lower than that quoted in larger series [6,7], but higher than the 5 to 6% quoted by Evans [10]. One explanation for the declining incidence may relate to the increased recognition of malignant fibrous histiocytoma.

The multiplicity observed in angiolipomas is well known [1]; 31 of our 58 patients harboring these tumors had an additional tumor excised. Such tumors pose no difficulty in histological diagnosis if their characteristic features are sought (see Figure 2).

In this study, middle-aged men were the dominant group (3:1). This is somewhat unusual, as previous reports indicate that ordinary lipomas are more common in females [1]. Most of the lipomas, excluding angiolipomas, were located on the trunk. Angiolipomas, however, were frequently located on the upper limbs and trunk, a previously noted feature [1]. Although two of the spindle-cell lipomas were located in unusual sites, their size and characteristic histological appearance aided in deciding the diagnosis. All pleomorphic lipomas in our series were also relatively small, as previously described [3,4]. However, the characteristic histological features, as shown in Figure 3, were present universally in only two lesions. In the remaining two, they were evident focally following examination of multiple sections. These findings illustrate the variability in the morphological expression of these rare neoplasms.

Histological diagnosis was not difficult in cases of renal angiomyolipoma or adrenal myelolipoma. In liposarcomas, the large size, necrosis, and gross invasion were valuable features, in addition to the presence of anaplasia and lipoblasts. The myxoid variants, with their characteristic capillary meshwork, were the easiest to diagnose while the most difficult were the round-cell type [6-10], though lipoblasts were identified in all cases. Pleomorphic liposarcoma is often confused with malignant fibrous histiocytoma due to the presence of numerous giant cells with deeply acidophilic cytoplasm [1]. None of the six liposarcomas, however, was classified as pleomorphic liposarcoma, thus avoiding this difficulty. The demonstration of lipoblasts is essential for diagnosing pleomorphic liposarcoma in such cases.

This study confirmed that TATO are the most common type of neoplasm encountered in clinical practice. Although the majority of these tumors are clinically insignificant ordinary lipomas, a small group remains that need to be segregated. Among these are the fairly common liposarcomas and the relatively rare lipoma variants that may simulate sarcomas. Correct diagnosis of these lipoma variants can prevent unnecessary surgery, worry, and confusion.

Acknowledgment

My gratitude to Miss Anelia Manzanilla for typing the manuscript and to Mr. M. Abdel Gadir and Mr. Abdel-Monem El-Tayeb for technical and photographic assistance.

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VITAMIN D DEFICIENCY RICKETS IN RIYADH

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على الرغم من صحو السماء في المملكة العربية السعودية معظم أيام السنة، إلا أن داء الرخد الناجم عن عوز فيتامين د غير نادر. تؤدي عوامل متعددة إلى هذه الظاهرة، وبخاصة العوامل الغذائية، والاجتماعية وعوز فيتامين د لدى الأمهات. تتناول هذه الدراسة ٥٠٠ حالة رخد من اجمالي ٢٧٢٣٦ مريض داخلي في مستشفى السليمانية للأطفال في الرياض على مدى ثلاث سنوات (١٩٨٦ إلى ١٩٨٨م). شكلت نسبة المرضى السعوديين ٨١٪ (متوسط أعمارهم ٨,٢شهرًا) وهذا يقل كثيرًا عن المشاهدات المألوفة. كان معظم المرضى يعانون في البداية من أعراض غير محددة، وذات علاقة غير مباشرة بعوز فيتامين د، وبخاصة تكرر أخماج الصدر (٦٦٪) والاختلاجات الناجمة عن تدني كلس الدم (١٧,٢٪).

كانت نسبة ٣٩,٢٪ من المرضى دون سن الستة أشهر، ونسبة ١٤,٢٪ من المرضى دون سن الثلاثة أشهر، وتعتبر هذه السن المبكرة لظهور الأعراض امرا غير عادي إذا قورن بالأعمار المقتبسة من المراجع الطبية. ويعود ذلك في غالب الظن إلى عوز فيتامين د لدى الأمهات. يبدو أن الأعراض السريرية الثانوية للرخد، والتي تم كشفها بالفحوصات شائعة الحدوث. خلاصة القول أن الرخد يشكل مشكلة صحية رئيسية في المملكة العربية السعودية تحتاج إلى مزيد من الاهتمام بكشفه، وعلاجه والوقاية منه.

Despite the fact that much of Saudi Arabia is sunny throughout most of the year, vitamin D deficiency rickets is not rare. Different factors are responsible for this phenomenon, especially nutritional, social, and maternal vitamin D deficiency. We identified 500 cases of rickets out of a total of 27,236 hospital admissions, and followed at Suleimania Children's Hospital in Riyadh over three years (1986 to 1988). Eighty-one percent of the patients were Saudi (mean age, 8.2 months), which is significantly lower than that usually observed. Most of the patients had nonspecific findings at onset, indirectly related to the vitamin D deficiency, particularly recurrent chest infections (66%) and hypocalcemic convulsions (17.2%). The young age at onset, which was 39.2% in patients younger than six months at onset and 14.2% in those younger than three months, is unusual compared with ages cited in the literature, and this most probably relates to maternal vitamin D deficiency. Subclinical forms of rickets, detected by the screening, also seem to be common. We conclude that rickets is a major health problem in Saudi Arabia and more attention needs to be paid to its detection, treatment, and prevention.

Vitamin D deficiency rickets is due to dietary factors and poor sunlight exposure. The incidence of vitamin D rickets is therefore usually low in sunny countries, but in Riyadh it is not rare.

We evaluated the factors associated with the development of rickets in our community, and discuss the preventive measures that should be adopted.

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Accepted for publication 15 February 1990.

Patients and Methods

Rickets was diagnosed in 500 patients (out of a total of 27,236 admissions) and patients were followed at Suleimania Children's Hospital in Riyadh over a period of three years (1986 to 1988).

Diagnosis was based on clinical (widened wrists and rosary rickets), radiological (rosary rickets, widening, cupping, fraying of distal ends of the ulna and radius), and biological (high alkaline phosphatase activity) findings. Furthermore, 1213 breastfed Saudi children below two years of age, seen in the outpatient clinic for nonspecific symptoms, were screened for rickets using x-ray studies of the wrist and measurement of alkaline phosphatase activity.

Nationality, sex, and age of the children were recorded, as were the nutritional status (breastfeeding, food diversification), sociofamilial status (residential location, type of housing, maternal age, educational level of parents, clothing styles), and history of exposure to sunlight.

Laboratory investigations included complete blood count, red blood cell morphology, calcium and phosphorus levels, and alkaline phosphatase activity. Chest and wrist x-ray studies were done in all patients.

X-ray wrist studies and determinations of alkaline phosphatase activity were also done in 76 sex- and age-matched control children, for whom nutritional status and history of exposure to sunlight were also recorded.

The dosage of hydroxylated vitamin D metabolites (25 hydroxy D_3 [25OHD] and 1.25 dihydroxy D_3 [1.25 DiOHD]) using a competitive protein-binding assay was determined in 188 Saudi children of both sexes; 103 were rachitic and 85 were control subjects, matched by age, who had had adequate nutritional and sunlight exposure and came from a sociofamilial background that would encourage these conditions.

Results

In our series, vitamin D deficiency rickets was seen in 1.83% of the total number of patients admitted during the three years. Of this group of rachitic patients, 81% were Saudi and 19% were non-Saudi (of these, 6.8% were Sudanese and 4.8% were Yemenite), 64.4% were male and 35.6% were female. Table 1 shows the age distribution in our patients, with a high prevalence seen in very young children. The age of onset ranged from 25 days to 2 years, 6 months (mean, 8.2 months). Among the 1213 breastfed children of both sexes screened, 85 (7%) were found to have subclinical rickets, based on an alkaline phosphatase value of at least 400 IU/L along with early metaphyseal changes (early cupping and irregular fraying). Alkaline phosphatase activity in our control children was 4.78 ± 1.12 μkat/L and local pediatric values ranged from 0.67 to 6.67 μkat/L [1,2]. X-ray studies of the wrists in control children were normal.

TABLE 1. *Age distribution.*

Age	Number	Percentage
0–1 mo	6	1.2
>1–3 mo	65	13
>3–6 mo	125	25
>6 mo–1 yr	228	45.6
>1–2 yr	72	14.4
>2 yr	4	0.8
Total	500	100

Sixty-seven percent of the patients were exclusively breastfed, compared with 42% of the control children; 31.8% had mixed alimentation (i.e., breastfed and adequate diversification), and six children (1.2%) who were not breastfed had rickets due to factors other than nutritional causes. About 50% of the patients lived in overcrowded areas and were affected by major sociocultural and educational problems. More than 50% of the patients lived in apartments or houses without a yard or garden and with high small windows, which did not allow for much exposure to sunlight. No patients lived in tents and 19.2% lived in traditional mud or brick houses. Finally, 72% of our patients (compared to 37% of the control children) were not exposed to sunlight. The majority of mothers (51.1%) considered sunlight harmful for the children; only 11.2% thought it beneficial. The maternal age in our series varied from 17 to 40 years (mean, 25.3 ± 5.9 years); 7.2% were 40 years or older. Illiteracy was found in 75.2% of the mothers. No comparable statistics were obtained for the control children. Most of the small infants were wrapped until they were six months old (Figure 1).

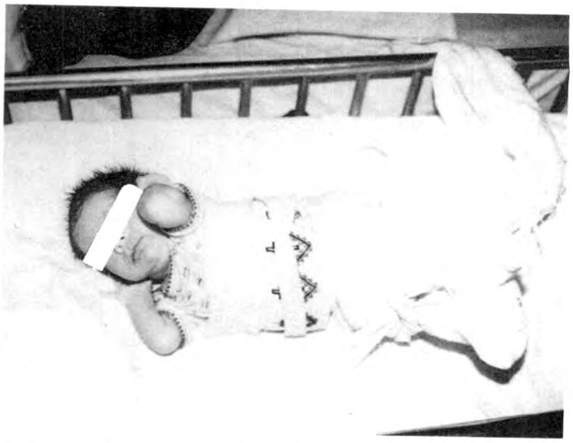

FIGURE 1. Wrapping of infant up to 6 months of age.

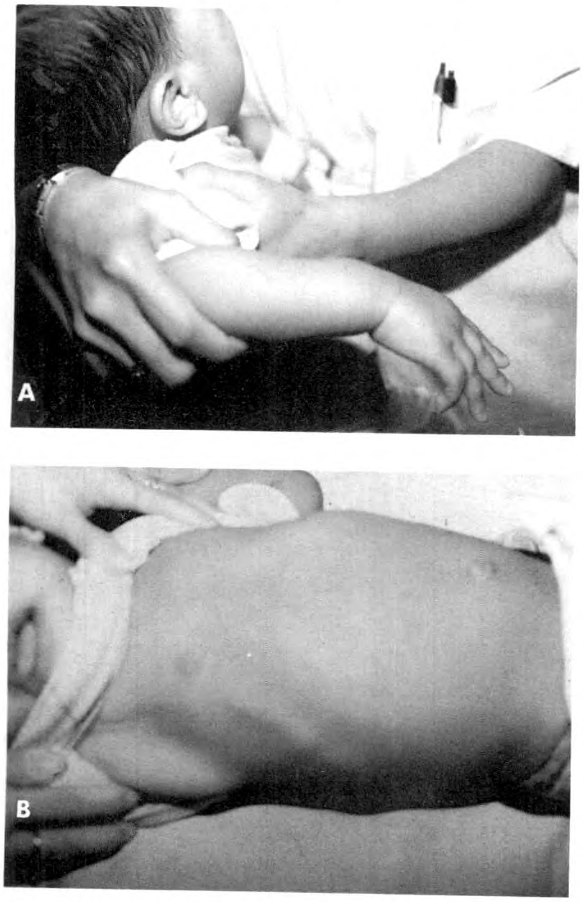

FIGURE 2. (A) Widened wrist. (B) Rosary rickets.

TABLE 2. *Classic signs and symptoms.*

Classic signs	Percentage
Widened wrists	82.5
Rosary rickets	44.2
Frontal bossing	27.7
Craniotabes	4.2
Fracture	0.2
Others	16.8

TABLE 3. *Vitamin D metabolites.*

	$25\ OHD_3$ (nmol/L)			$1.25\ DiOHD_3$ (pmol/L)	
Patients	No.	Mean	Range	Mean	Range
Male					
Rachitic	78	17.2	7.2–27.2	7.1	2.2–11.9
Control	54	41.6	15.4–67.8	13.5	2.6–20.1
Female					
Rachitic	25	18.4	6.2–36.2	7.2	3.1–11.3
Control	31	47.1	12.4–81.8	14.7	6.2–23.2

$25\ OHD_3$ = 25 hydroxy D_3; $1.25\ DiOHD_3$ = 1.25 dihydroxy D_3

More than 75% of the patients presented at onset with symptoms indirectly related to rickets, especially recurrent chest infection (66%) and hypocalcemic convulsions (17.2%) in younger infants. Other findings were variable and not characteristic (e.g., delayed walking, delayed teething, gastrointestinal symptoms), occurring in 16.6%.

Classic signs and symptoms were found in a variable percentage of the patients (Figure 2, Table 2). X-ray studies of the wrist and chest showed the classic bone changes (Figures 3 to 5) [3]. These bone changes were seen in the first months of life in some patients. This, in association with the high alkaline phosphatase activity in breastfed infants, is important, although rickets in its earliest stage is not usually detected radiologically [3]. Cupping of the distal end of the ulna in young infants is not necessarily abnormal, and has been observed in some nonrachitic children during the first months of life [3]. The x-ray studies of the wrists in our control children were normal, however. There were low calcium and phosphorus levels in 17.2% and 14.8% of the patients, respectively, and a high alkaline phosphatase activity in all patients (range, 0.34–170.2 μkat/L). Microcytic hypochromic anemia was seen in 57 patients (8.79%), most of them aged one year or less. The levels of vitamin D metabolites 25 OHD and 1.25 DiOHD were significantly lower in the patients of both sexes than those in the controls (Table 3), but our results for 25 OHD seem higher than those reported in previous studies (9.23 ± 5.74 nmol/L) [4,5,10]. However, they are still significantly different from the values observed in control groups.

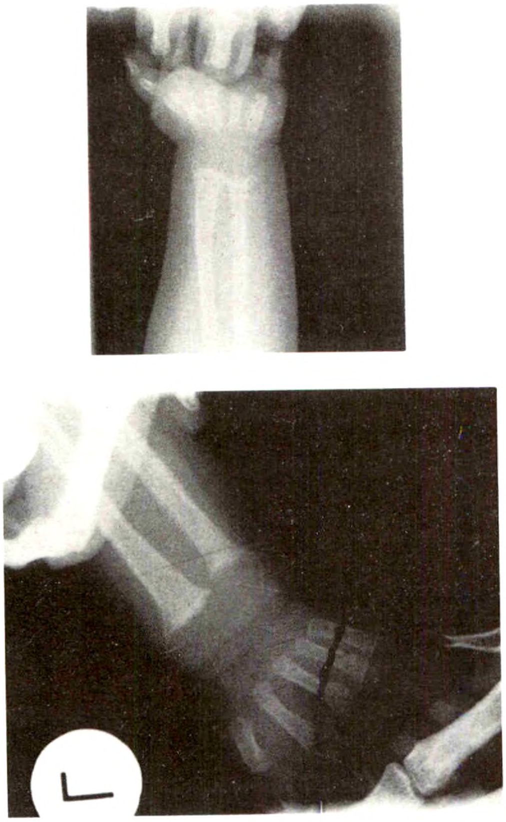

FIGURE 3. Bone changes seen in the first months of life.

Other authors have reported lower levels of 25 OHD for both Saudi adult patients (7.98 ± 5.74 nmol/L) and for normal controls (8.98 ±5.74 nmol/L), compared with control values obtained from Western subjects (42.68 ± 24.21 nmol/L) [10], and higher values seen in the rural population (10.43 ± 7.03 nmol/L) than in the urban one (7.83 ± 5.29 nmol/L) [10]. No study of 1.25 DiOHD levels in Saudi rachitic and nonrachitic children has been conducted.

Most of our patients (98.6%) had vitamin D deficiency rickets that was due to nutritional factors. Other causes (liver disease [0.4%], anticonvulsant therapy using agents such as phenytoin [0.2%], and vitamin D resistant rickets [0.8%]) were rare.

Discussion

Rickets is a relatively common disorder in Riyadh and has been attributed to several factors. Saudi children are breastfed for usually the first two years of life, without adequate nutritional diversification [4,5] as shown in our series. It is well known that maternal milk, as a unique source of vitamin D, does not supply enough of the daily requirements for the children [6,7]. This is even more true when the mothers are already deficient in vitamin D. Vitamin D deficiency in Saudi mothers has been proved in several studies [4,5,8–10]. The 25 OHD levels were found to be low in pregnant women and in lactating mothers and were significantly lower than those measured in Western women or women from other Arabian countries who were living in the Kingdom [5,8]. These results have a greater consequence when considering the almost continuous cycle of pregnancies and lactation of Saudi mothers. All these elements explain the presence of obvious clinical

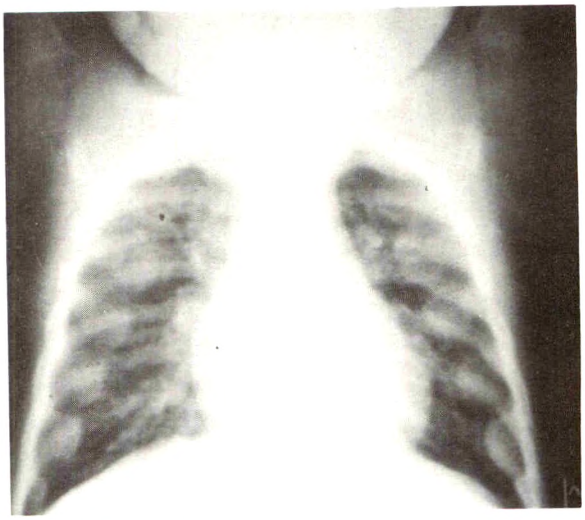

FIGURE 4. Rosary rickets.

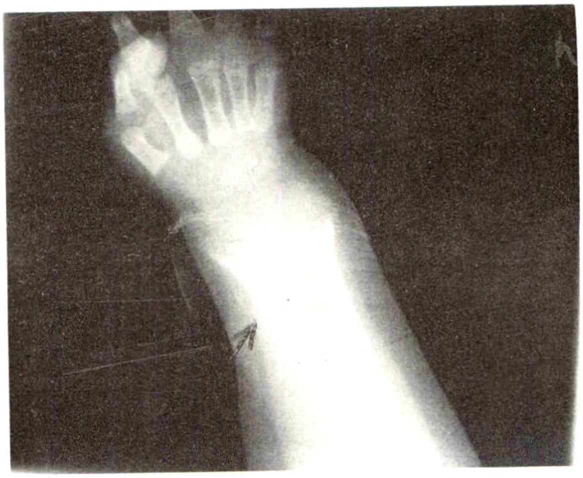

FIGURE 5. Wrist fracture.

and radiological signs of rickets in Saudi children during the first months of life. The mean age at onset of symptoms and signs in our series was 8.2 months, compared with 11 months quoted in other similar local studies [4,5] and with those reported elsewhere in the literature.

Saudi children do not get much exposure to sunlight, and this is due to such local factors as housing design and clothing styles, as well as the strong tendency to avoid sunshine and heat. It has been proved that, despite frequent haze and sandstorm, there is no significant seasonal variation in the ultraviolet light reaching the earth's surface in the Kingdom [11–13]. No genetic factor (invoked initially) seems to be involved in the pathogenesis of the disease. Subclinical forms of rickets also seem to be common, as shown by the results of outpatient screening in breastfed children.

Because of the relative frequency of vitamin D deficiency rickets in Riyadh, a concerted effort must be made to screen breastfed children to detect subclinical forms of rickets and to educate the public about the importance of sunlight exposure and diversified nutrition. We consider vitamin D supplementation the most appropriate measure to prevent rickets, both for children during the entire time of breastfeeding and for pregnant and lactating mothers.

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CROHN'S DISEASE IN ARABS

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يذكر داء كرون على نطاق واسع في الكتابات الغربية ولكنه لم يشاهد كثيرًا في مجتمعات الشرق الأوسط. شخصنا داء كرون لدى سبعة مرضى عرب، كان ثلاثة منهم سعوديين وكان العمر المتوسط لهم ٣٢,٤ سنة (المدى ١٨ - ٤٠ سنة). تفاوتت فترة ظهور الأعراض من ثلاثة أشهر إلى عشر سنوات. كان موقع المرض لفائفي قولوني لدى خمسة مرضى وقولوني لدى مريضين. شوهدت كتل في البطن لدى ثلاثة مرضى. شخصت أربع حالات بفحص العينات النسيجية المأخوذة أثناء تنظير القولون. وجدت مظاهر غير معوية لدى ثلاثة مرضى. كانت الجراحة علاجًا كافيًا لدى مريضين في حين لزم العلاج الطبي للآخرين وبخاصة الستيرويدات مع الجراحة أو بدونها. ونستخلص من هذه الدراسة أن مرض كرون موجود لدى الجمهور العربي ولكن تأثيراته المجموعية أخف.

Crohn's disease is widely described in the Western literature, but it has not been widely observed in the Middle Eastern community. We diagnosed Crohn's disease in seven Arabs, three of whom were Saudi Nationals. Their mean age was 32.4 years (range, 18–40 years) and duration of symptoms varied from three months to ten years. The site of the disease was ileocolic in five patients and colonic in two. Mass lesions in the abdomen were seen in three patients. Four cases were diagnosed from histological specimens obtained at laparotomy and resection and the other three were diagnosed from colonoscopic biopsy specimens. Extraintestinal manifestations were found in three patients. Surgery alone was the treatment in two patients, whereas the remaining required medical therapy, mainly steroids, with or without surgery. We conclude that Crohn's disease does occur in the Arab population, but with milder systemic effects.

Crohn's disease is a relatively common disorder in Western populations [1], whereas tuberculosis of the intestine is more frequently seen in the populations of developing countries [2]. The diseases have similar presentations, making diagnosis difficult [3]. There are only scanty reports of Crohn's disease from the Middle East [4,5]. We report here on seven Arabs with Crohn's disease and describe their clinical presentations, compared with those described from the West.

Case Reports

Patient 1

A 35-year-old married Saudi woman had had recurrent bouts of diarrhea with abdominal pain, fever, and weight loss over the course of six months. She also had intolerance to milk and dairy products.

Examination revealed a febrile and pale woman. Abdominal examination showed central distention with diffuse tenderness. Her hemoglobin was 90 g/L and erythrocyte sedimentation rate (ESR) was 52 mm in the first hour. Repeated stool examinations failed to show any ova, cysts, or parasites, and stool cultures were negative. Liver function tests showed low albumin concentration with raised alkaline phosphatase activity. A small-

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Accepted for publication 17 March 1990.

bowel enema showed multiple strictures with dilatation of the proximal ileal loops.

Because of the deterioration in her general and nutritional condition, intestinal tuberculosis was suspected.

Laparotomy was performed and this showed thickened intestinal loops with adhesions. The patient underwent resection of the terminal ileum with limited right hemicolectomy. The resected segments of the small bowel showed transmural inflammation with involvement of the serosa, and noncaseating granulomata, with mucosal ulceration revealed by microscopic examination. No bacilli were noted on Ziehl-Neelsen staining. Culture of the tissue did not show growth of acid-fast tubercle bacilli. The histopathology was consistent with the active stage of Crohn's disease. She was treated with parenteral nutrition and systemic corticosteroids.

Postoperatively an enterocutaneous fistula developed and required another laparotomy for resection of the fistula. Subsequently she was readmitted because of recurrent diarrhea and fever. Further radiological studies indicated that she had a retrocecal abscess (Figure 1), which was drained surgically. She has been followed closely in the medical clinic for four years, and her minor relapses have been controlled by medical treatment.

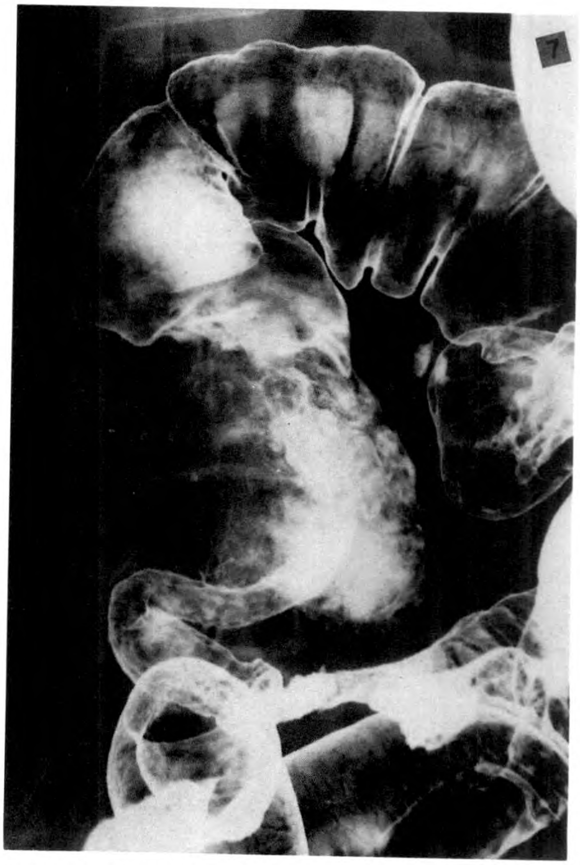

FIGURE 1. Patient 1. Small-bowel enema study showing narrowing of the terminal ileum with retrocecal abscess formation.

Patient 2

An 18-year-old single Saudi woman presented with right-sided abdominal pain, intermittent diarrhea, fever, weight loss, and amenorrhea that had lasted for 1 year. On one occasion she passed fresh blood per rectum. She had undergone an appendectomy 18 months prior to admission at King Khalid University Hospital, Riyadh. On examination she was found to be thin, pale, and pyrexial (38.5±C). Cautery and appendectomy scars were noted on abdominal examination. There was tenderness and guarding over the right iliac fossa. Rectal findings were unremarkable. Her hemoglobin level was 78 g/L; white cell count, 12.0×10^9/L; and ESR, 82 mm in the first hour. Stool examination was positive for occult blood. Repeated stool examinations did not show ova, cysts, or parasites. Blood cultures were negative. Repeated colonoscopic examinations showed nonspecific colitis and no evidence of granuloma or acid-fast bacilli in the submitted tissue. A small bowel enema revealed marked edema of the cecum, multiple ulcers, and a deep irregular fistulous tract extending from the hepatic flexure to the subhepatic space. A computed tomographic scan of the abdomen showed a large right abdominal mass. In view of these findings, intraabdominal tuberculosis was suspected.

Laparotomy was performed and revealed a nonsuppurating mass extending from the subhepatic area to the pelvis, consisting of the whole of the cecum and the ascending colon, which showed transmural thickening. A right hemicolectomy and ileotransverse anastomosis of the normal-looking bowel was carried out. Histological examination of the resected bowel showed ulcerative fissuring and transmural noncaseating granuloma with foreign-body giant cells. No acid-fast bacilli were seen or cultured from the resected tissue. A diagnosis of Crohn's disease was made.

Her postoperative course was uneventful. She was followed for three years. During that time she gained 20 kg and her menses became regular.

Patient 3

A 40-year-old Saudi woman had experienced right-sided abdominal pain with intermittent rectal bleeding for three months, with a weight loss of 3 kg. Twelve years before she had undergone appendectomy, and four years previously, spinal fusion of the fifth lumbar and first sacral vertebrae to correct spondylolisthesis, which was performed in another country.

There was tenderness on palpation of the right iliac fossa. Her hemoglobin concentration was normal with a mild leukocytosis. Repeated stool examinations, including cultures, were normal. Colonoscopic examination revealed a large irregular ulcer in the cecum, with multiple small satellite ulcers in the cecum and over the ileocolic valves. Multiple endoscopic specimens were obtained, and histological examination showed a nonspecific ulcer without granuloma. Her symptoms did not resolve, so surgical exploration of the abdomen was done because of suspected malignancy. At operation the cecum was noted to be indurated and thickened. The cecum and 5 cm of the terminal ileum were resected, and an ileocolic anastomosis was made.

Macroscopic examination showed edema and superficial ulceration of the mucosa. Histological examination revealed patchy ulceration and chronic inflammatory cell infiltrate with edema of the entire wall. There was lymphoid aggregate and marked lymphoid hyperplasia in the nonulcerated area, considered indicative of Crohn's disease.

The patient required no subsequent medication and made an uneventful recovery.

Patient 4

A 35-year-old Egyptian man presented with chronic diarrhea, intermittent rectal bleeding, and weight loss. Four years previously he had undergone an appendectomy at another hospital.

On examination, finger clubbing and bilateral peripheral arthritis were observed and two anal tags were found per rectum. His hemoglobin concentration was normal. Repeated stool examinations were negative for an infective organism, but barium enema showed the terminal ileum was narrowed and the ileocecal region was deformed. Colonoscopy indicated multiple patchy, superficial ulcerations in the colon with friable mucosa. Microscopic examination of the colonic biopsy specimens showed chronic inflammatory ulceration, crypt abscess, and noncaseating granuloma. Acid-fast bacilli were not seen or cultured from the colonic tissue.

Treatment with systemic corticosteroids and metronidazole was initiated but the patient was lost to follow-up.

Patient 5

A 35-year-old Moroccan man was admitted because of recurrent diarrhea, rectal bleeding, and abdominal pain of ten years' duration. These symptoms had worsened in the preceding two months and were accompanied by fever and weight loss. He was a heavy smoker.

On admission he was found to be pyrexic and had tenderness along the left side of the colon. Digital examination of the rectum revealed tenderness, and the examiner's fingertip was blood-stained.

Several stool examinations for infective organisms were negative. His hemoglobin level was normal but ESR was elevated. Serological examination for amebiasis and schistosomiasis as well as blood cultures were negative. A barium study of the colon showed a thickened colonic wall with narrowed lumen, deep ulcerations, and pseudopolyp formation with a "cobblestone" pattern in some areas (Figure 2). Colonoscopy confirmed the radiological findings. Histological analysis of the submitted tissue showed depletion of the goblet cells along with submucosal edema with small focal areas of ulceration.

Treatment was initiated with systemic corticosteroids and his symptoms abated. The patient was subsequently lost to follow-up.

Patient 6

A 29-year-old Lebanese man presented with a five-year history of intermittent watery diarrhea and colicky abdominal pain. On occasion he passed blood-stained stool. He was a smoker. He often used antacids and Ranitidine for abdominal pain but without relief. He was seen at several hospitals and by many physicians, for the problem. Two months prior to admission to King

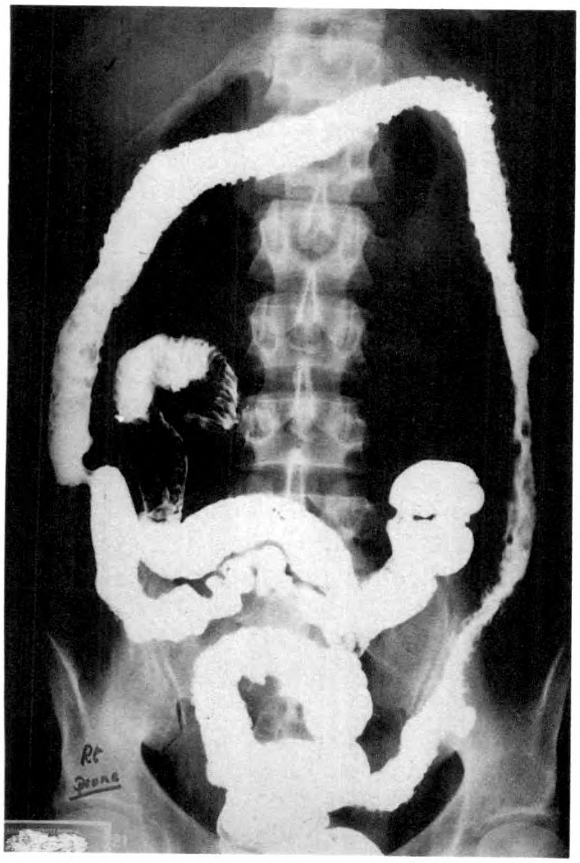

FIGURE 2. Patient 5. Barium enema study showing lack of haustration of the colon, narrowing of the colonic lumen, and deep ulcerations.

Khalid University Hospital his symptoms worsened. His hemoglobin concentration was normal. A small-bowel enema showed rapid transit of the barium through the small bowel and diffuse narrowing of the terminal ileum.

During admission examination a palpable tender mass (10 × 12 cm) was found in the right iliac fossa. Repeated stool examinations failed to show any infective organisms. Other laboratory findings were essentially normal. Tuberculin skin testing was negative. Chest x-ray study was normal. A small-bowel series demonstrated diffuse narrowing of the ileum with displacement by extraluminal masses and edema, thumb printing, and ulcers of the mucosa, a picture that was highly suggestive of Crohn's ileitis. However, colonoscopic findings up to the cecum were normal. At laparotomy, generalized thickening of the small bowel was found along with multiple stenotic lesions and a mesenteric mass. Ten centimeters of the terminal ileum was resected and the luminal surface showed patchy ulceration and strictures (Figure 3).

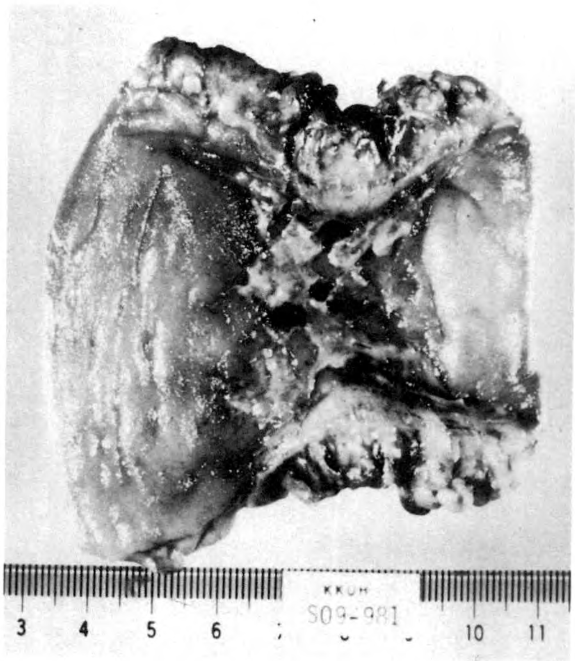

FIGURE 3. Patient 6. Resected specimen of the terminal 10 cm of ileum showing transmural involvement with patchy ulcerations and stricture.

Histological examination showed transmural chronic inflammatory cells, ulcerations, and multiple noncaseating granulomas (Figure 4). The mesenteric mass consisted of fat and lymphoid tissue with noncaseating granulomas. No acid-fast bacilli were seen.

The patient was treated with parenteral nutrition for two weeks, followed by orally administered corticosteroids. His symptoms abated over the next three weeks and he was followed through the medical clinic at regular intervals for 18 months without any relapse. Apart from soft stool, he remained asymptomatic while on maintenance corticosteroid therapy.

Patient 7

A 35-year-old Syrian man had suffered from psoriasis for 18 months and been receiving corticosteroids irregularly. For three months the patient had experienced intermittent diarrhea with abdominal pain. He denied any history of fever, night sweats, or laxative abuse. He felt pain in the low back, wrists, and both knee joints. He often took metronidazole tablets to control his diarrhea.

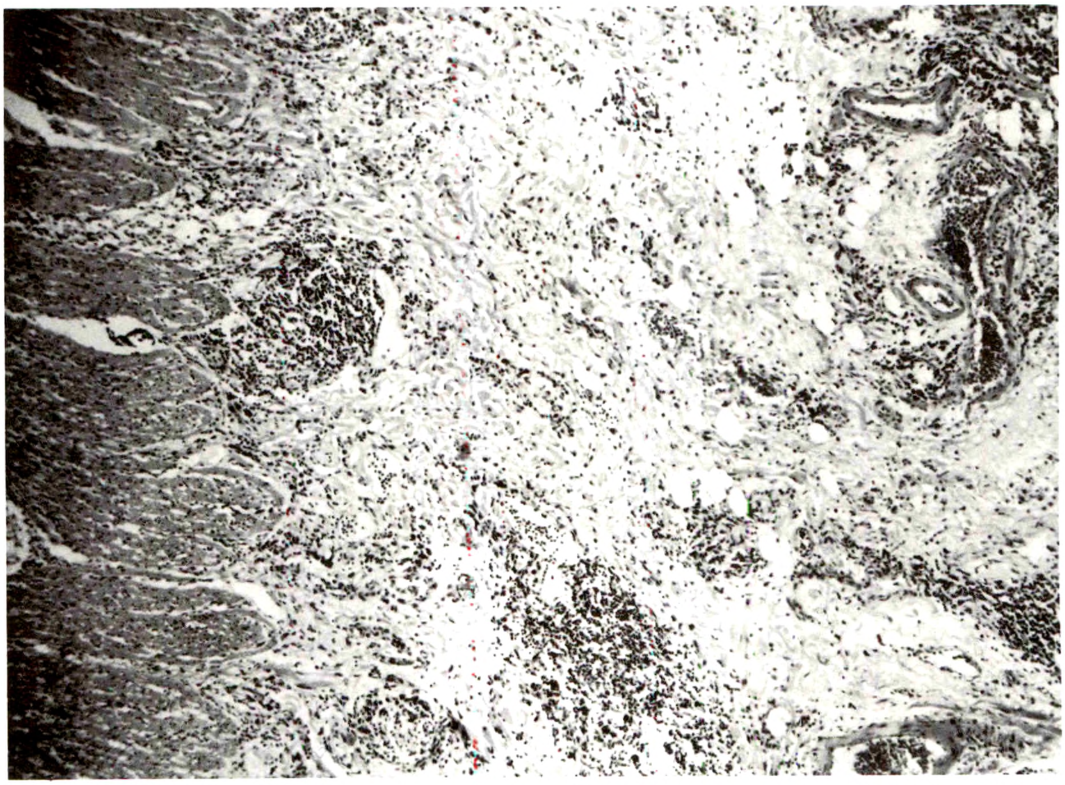

FIGURE 4. Patient 6. Histological appearance of resected bowel showing chronic inflammatory cells, ulcerations, and multiple noncaseating granulomata (H&E, original magnification, × 400).

On examination, extensive psoriatic lesions were noted on the limbs and over the trunk. Bilateral finger clubbing was observed. There was diffuse tenderness of the lower abdomen. Laboratory investigations revealed anemia (hemoglobin, 96 g/dL) with a raised ESR of 123 mm in the first hour. Repeated stool examinations did not show ova, cysts, or parasites. Chest x-ray study was normal. On radiological examination there was evidence of right-sided sacroileitis. Colonoscopy indicated hyperemia extending from the sigmoid colon to the terminal 30 cm of ileum with rectal sparing. Histological analysis of biopsy specimens from the colon and terminal ileum showed chronic inflammatory cells, ulcerations, and crypt abscess, while the specimens from the rectal biopsy appeared normal. The histological appearance was highly suggestive of chronic inflammatory disease. In view of the rectal sparing and involvement of the terminal ileum, Crohn's disease was diagnosed.

The patient was treated with bowel rest for one week. Initially he was given parenteral steroids, and once his symptoms abated, oral steroids were commenced. His symptoms gradually eased over the next three weeks and he was discharged from the hospital with regular follow-up in the clinic.

Discussion

Recently Kirsner et al [1] observed that inflammatory bowel disease is rare or nonexistent in Saudi Arabia and Morocco, though there are a few reports from Saudi Arabia and Kuwait [4-6]. Seven of 495 Arab patients who had colonoscopic examinations over a period of six years at the King Khalid and King Abdulaziz University Hospitals, Riyadh, were found to have Crohn's disease of the bowel.

Our patients' ages ranged from 18 to 40 years (mean, 32.4 years). This finding is compatible with those reported from Ireland and the U.S. [7,8]. Four of our patients were males and three were females. Three were Saudis, all females.

There was a delay in diagnosis of between three months and ten years. This may be due to lack of

TABLE 1. *Cardinal clinical features of eight Arab patients with Crohn's disease.*

Data	1	2	3	4	5	6	7
Age (yr)	35	18	40	35	35	29	35
Sex	Female	Female	Female	Male	Male	Male	Male
Nationality	Saudi	Saudi	Saudi	Egyptian	Moroccan	Lebanese	Syrian
Diarrhea	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Rectal bleeding	No	Yes	No	No	Yes	Yes	No
Abdominal pain	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Weight loss	Yes	Yes	No	Yes	Yes	Yes	Yes
Fever	Yes	Yes	No	Yes	Yes	–	–
Anemia	Yes	Yes	No	No	No	No	Yes
Abdominal tenderness	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Abdominal mass	Yes	Yes	No	No	No	Yes	No
Clubbing	Yes	No	No	No	No	No	Yes
Arthralgia	No	No	Yes	Yes	No	No	Yes
Erythema nodosum	No	No	No	No	No	No	No
Site of bowel disease	Ileocolic	Ileocolic	Ileocolic	Ileocolic	Colon	Ileocolic	Colon
Complications	Paracolic abscess and fistula	Non-suppurating mass of colon & fistula	Cecal ulcer	None	None	Mass in abdomen	None

awarenesss among physicians, as infective diarrhea is a common ailment in developing countries. It is common to prescribe multiple antibiotics and antiamebic drugs without considering the possibility of noninfective causes of chronic diarrhea.

Cardinal clinical features (Table 1) were: diarrhea, abdominal pain, and weight loss. All our patients experienced abdominal pain during the course of the disease. This is not only due to the inflammatory process of the disease, but there were luminal obstructions in the small bowel in five patients and colonic involvement was noted in another two patients. The disease was limited to the ileocolic region in five patients, with colonic involvement in two patients. Our findings agree with those from a larger study [8], which found that the most common anatomical site is ileocolic.

Three patients suffered local complications consisting of fistula and abscess formation. Systemic involvement, such as arthritis and finger clubbing, was observed in three patients. These features were suggestive of active disease [7]. We did not note mouth ulcers, erythema nodosum, iritis, or nephrolithiasis in any of our patients in contrast to observations from Western series [9,10].

Barium studies of the small intestine indicated luminal narrowing and edema in five patients, and multiple ulceration and fistulae were noted in two patients. These findings are consistent with those in the study of Goldberg et al [11].

Patient 1 had relapse of the disease following resection of the small bowel, which was done for both therapeutic and diagnostic reasons. Enteroenteric and entercutaneous fistulae developed which necessitated further surgical intervention. It is known that the recurrence rate following resection is as high as 78%, and particularly so following the second surgical resection [12].

Tuberculosis of the intestine is more commonly seen in developing countries [2], and clinically and radiologically may mimic Crohn's disease. Because of this overlap, even on endoscopic and histological examination, it may be extremely difficult to differentiate between tuberculosis of the intestine and Crohn's disease.

It is important to examine the biopsied tissue for the presence of acid-fast bacilli, both on Ziehl-Neelsen staining and culture of the tissue. In fact, we excluded one patient from this series as the patient was initially considered to have Crohn's disease of the colon based on history, clinical examination, colonoscopy, and histological findings.

Shortly after Crohn's colitis was diagnosed, the patient was lost to follow-up. Two years later she returned because the diarrhea had worsened. On this occasion, tissue specimen obtained at colonoscopy revealed positive acid-fast bacilli on Ziehl-Neelson staining and tissue culture grew *Mycobacterium tuberculosis*.

All our patients had active disease at diagnosis and were admitted for two to four weeks for bed rest and intravenous fluid replacement. Bowel rest was given and any electrolyte deficit was corrected. Three patients required blood transfusions because of blood loss. Parenteral nutrition was required for two patients in preparation for surgery. Sulfasalazine was used in two patients with Crohn's colitis. Short-term corticosteroid therapy was necessary in seven of our patients.

Five of our patients required surgery for diagnostic and therapeutic reasons. We did not observe any malignancy in association with Crohn's disease during the short follow-up period, which was between 6 and 60 months (mean, 18 months). Two patients were lost to follow-up when they left Saudi Arabia.

We conclude that Crohn's disease does exist in Arabs, although the true incidence is not known. The clinical pattern of this condition appears similar to that observed in the West, with the exception of less severe systemic effects. A large multicentre and longitudinal study is required before any tangible conclusions can be drawn regarding the epidemiology and clinical pattern of Crohn's disease in Arabs.

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PATTERN OF DIABETIC FOOT LESIONS IN SAUDI ARABIA: EXPERIENCE FROM KING KHALID UNIVERSITY HOSPITAL, RIYADH

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أجريت دراسة مراجعة لتقدير حجم مشكلة آفات القدم ونماذجها لدى مرضى السكري في المملكة العربية السعودية. وقد أظهرت مراجعة ملفات ألف وعشر مرضى بالسكري في مستشفى الملك خالد الجامعي بالرياض انتشارا إجماليًا لآفات القدم لدى المرضى بنسبة ١٠,٤٪. تم تصنيف ٨٨ من هؤلاء المرضى بشكل أوسع فتبين أن ٥٥ منهم (٦٢,٥٪) كانوا من الذكور و ٣٣ (٣٧,٥٪) كنّ من الاناث. وكان عدد السعوديين منهم ٧٥ (٨٥,٢٪) مريضًا بينما كان ثلاثة عشر مريضا (١٤,٨٪) من غير السعوديين. وكان متوسط العمر ٥٨ عامًا. تبين أن خمسة وثمانين مريضا مصابون بداء السكري من النمط الثاني وثلاثة فقط من النمط الأول. شمل الطيف السريري لآفات القدم عشر حالات من التهاب الهلل. وثلاثة وثلاثين قرحة وتسعة وعشرين حالة موات وستة عشر خراجا. كانت علامات اعتلال الأوعية المحيطية ظاهرة لدى ثمانية وأربعين مريضا (٥٤,٥٪) فيما وجد اعتلال الأعصاب المحيطية لدى ثلاثة وأربعين مريضا (٤٨,٨٪). أجري إنظار جراحي مع تضميد طويل المدى على ثمانية وخمسين مريضا (٦٦٪) بينما أجري البتر لثلاثين مريضا (٣٤,١٪). وبلغ معدل المكوث في المستشفى ٦,٨ أسبوعا. تعتبر آفات القدم السكرية من المضاعفات الرئيسية لهذا الداء في المملكة العربية السعودية. كما أن ارتفاع معدل البتر يدعو إلى القلق، والحاجة ماسة لذا لتطوير الوسائل التي من شأنها الإقلال من هذه العواقب الخطيرة.

A retrospective study was carried out to estimate the magnitude and pattern of foot lesions seen in diabetics living in Saudi Arabia. A review of the records of 1010 diabetic patients seen at King Khalid University Hospital, Riyadh, revealed an overall prevalence of 10.4% for diabetic foot lesions. Of these, 88 patients were further characterized; 55 (62.5%) were males and 33 (37.5%) were females. Seventy-five patients (85.2%) were Saudis and 13 (14.8%) were non-Saudis. The average age was 58 years. Eighty-five patients had type 2 diabetes and three had type 1. The spectrum of foot lesions included: 10 cases of cellulitis, 33 cases of ulcers, 29 cases of gangrene, and 16 cases of abscess. Evidence of peripheral vascular disease was present in 48 patients (54.5%) while peripheral neuropathy was found in 43 (48.8%). Surgical debridement with prolonged dressing was done in 58 patients (66%) while amputation was performed in 30 (34.1%). The average hospitalization was 6.8 weeks. Diabetic foot lesions constitute a major complication of this disease in Saudi Arabia. The high amputation rate is a source of concern and improved techniques are urgently needed to reduce this serious outcome.

Despite the tremendous advances in the management of diabetes mellitus, diabetic foot lesions continue to be a major problem in this disease [1–3]. It has been estimated that 20% of all diabetic admissions to hospital are for the treatment of foot lesions [4]. In the U.S.A., hospital costs related to

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Accepted for publication 24 March 1990.

diabetic foot disease have reached a record high of 200 million dollars per year [1]. In the U.K., the estimated cost for performing an amputation and the subsequent patient care is £9400 [5]. Diabetic foot admissions account for 47% of all admission days, reflecting the usually long hospital stay [5].

Diabetes mellitus has emerged as a major public health problem in Saudi Arabia, demanding effective strategies for diagnosis and early proper management [6]. Although some aspects of the disease have been described, the pattern of diabetic foot disease in Saudi Arabia has not been documented previously. The present study was undertaken to estimate the magnitude of the problem and to establish the important clinical, biochemical, and microbiological features of these lesions.

Material and Methods

A retrospective review of the case files of all hospitalized and ambulatory diabetic patients seen at the King Khalid University Hospital between 1983 and 1989 was undertaken. The records of all those who were diagnosed as having diabetic foot lesions were analyzed for the following: clinical variables which included demographic profiles of the patients; type of diabetes; its duration and treatment methods; presence of complications of diabetes (especially peripheral vascular disease and peripheral neuropathy); the side, site, and nature of the foot lesions; radiological findings; microbial flora of the lesions; biochemical and hematological data; and management of the lesions.

Results

A total of 1010 patient records were reviewed and 105 patients with diabetic foot lesions were identified, yielding an overall prevalence of 10.4%. Complete data for analysis were available in only 88, and only these 88 patients were studied.

There were 55 (62.5%) males and 33 (37.5%) females. Seventy-five patients (85.2%) were Saudis while 13 (14.8%) were non-Saudis. The overall mean age of the patients was 58.9 ± 8.6 (range, 45–83) years. Eighty-five patients (96.6%) had type 2 diabetes and 3 (3.4%) had type 1. All type 1 diabetics were on insulin therapy. Of the 85 type 2 patients, 16 (18.2%) were controlled on diet, 51 (58%) were on oral hypoglycemic agents, and 18 (20.5%) were on insulin. The overall mean duration of disease was 152 months to 67 years (range, 1–30 years).

TABLE 1. *Foot lesions among diabetic patients in Saudi Arabia.*

Lesion	No. of cases	Percentage
Ulcers		
Neuropathic (painless)	13	14.7
Neuroischemic (painful)	6	6.8
With cellulitis	14	15.9
Gangrene		
Alone	13	14.7
With an ulcer	4	4.5
With cellulitis	12	13.6
Abscesses		
Alone	14	15.9
Abscess with ulcer	2	2.3
Cellulitis, alone	10	11.4
Total	88	100

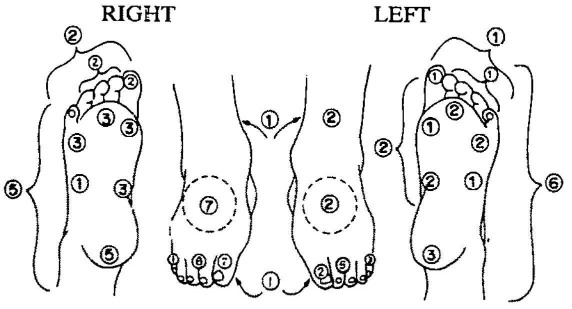

FIGURE 1. Sites and frequencies of foot lesions in the 88 diabetic patients.

Clinical evidence of peripheral neuropathy was present in 43 patients (48.8%). Peripheral vascular disease, which was assessed only clinically by palpation of the dorsalis pedis and posterior tibial arteries, was present in 48 patients (54.5%), though the serious limitation in this approach is acknowledged. A known history of trauma was identified in only 15 patients (17%). Twenty-seven patients (30.7%) had a past history of foot lesions. Cataract was evident in 38 (43.2%), diabetic retinopathy in 33 (37.5%), and proteinuria (> 0.5 gm/24 hours) in 35 (39.7%).

Table 1 and Figure 1 summarize the different types and sites of foot lesions encountered in the 88 cases. Both limbs were involved to a similar extent and the distribution of lesions was also nearly identical. No part of the foot was spared

TABLE 2. *Bacteriological findings in 88 cases of diabetic foot lesions.*

Culture results	No. of cases	Percentage
Negative cultures	29	33
Single organism:	27	30.7
Staph. aureus	12	
Proteus mirabilis	4	
Pseudomonas aeruginosa	3	
E. coli	2	
Group B beta hemolytic streptococcus	2	
Klebsiella	1	
Citrobacter diversins	1	
Enterobacter cloacae	1	
Streptococcus faecalis	1	
Multiple organisms*	31	35.2

*Most commonly *Staph. aureus, B hemolytic streptococci, Pseudomonas, E coli, Klebsiella, Proteus,* and bacteroides.

and lesions that involved the whole foot were present in 11 (12.5%) patients. Of the 43 patients who had foot x-ray studies, osteomyelitis was present in 16 (37.2%) and gas in the tissue space was seen in seven (16.3%). No foreign bodies were seen.

The mean random blood glucose level at presentation was 16.8 mmol/L (range, 5.3–30.2 mmol/L) and the mean white cell count was 15.1 (range, 4040–31,000) per cubic millimeter. HbA1c was not measured in most of the cases. Swabs taken from lesion sites were positive for organisms in 57 cases (64.8%). Multiple organisms (aerobic and anaerobic) were isolated in 31, while one organism was isolated in 26. Among the 63 patients who had blood cultures done, positive cultures were obtained in only two (3.2%). Table 2 summarizes the bacteriological isolates from the lesions.

Surgical debridement with prolonged dressing was done in 58 cases (65.9%), while amputation was performed in 30 (34.1%). Six patients refused amputation. Of the 30 patients who had amputation, 24 (80%) were males and six (20%) were females (age range, 45–75 years; mean, 60.3 ± 9.7 years). The average overall hospitalization was 6.8 weeks, and the average hospitalization in those undergoing amputation was 8.1 weeks. Table 3 summarizes the sites and extent of the amputations. A total of 16 patients (53.3%) had whole-limb amputation.

Discussion

Our study revealed a frequency of 10.4% of documented diabetic foot lesions among our diabetic population. Minor lesions may have been missed, as it has been shown that only 12% of diabetic patients routinely have foot examinations when in diabetic clinics, and this could mask the actual number of diabetic patients with foot lesions [7]. Our data identified elderly type 2 male diabetic patients to be particularly at risk. This is clearly reflected in both the total number of cases and those who had amputation.

There was an association of diabetic foot lesions with the occurrence of both peripheral vascular disease and peripheral neuropathy, as has been reported previously [8–9]. However, the unreliability of the method used to assess peripheral vascular disease in this study must be acknowledged. The Doppler ultrasound flow study is noninvasive and is more sensitive for such assessments. The high prevalence of ocular lesions, namely cataract and marked retinopathy, is relevant, as diminished vision can lead to a greater likelihood of injuries. There is a high amputation rate in our series and several explanations can account for this. Many patients presented very late, thereby making it impossible to save their feet. It is also possible that conservative management was not aggressive or persistent enough. None of the patients had total contact casting done for their lesion, which has recently been reported to be more effective in the treatment of plantar ulcers

TABLE 3. *Site and extent of amputation in 30 cases of foot lesions.*

	Toes					
Side	2nd–5th	Big toe	Foot	Below knee	Above knee	Total
Right	5 (16.6%)	3 (10%)	0	1 (3.3%)	5 (16.6%)	14 (46.7%)
Left	5 (16.6)	0	1 (3.3%)	5 (16.6%)	5 (16.6%)	16 (53.3%)
Total	10 (33.3)	3 (10%)	1 (3.3%)	6 (20%)	10 (33%)	30 (100%)

then traditional dressing treatment [10].

It is likely that some of the patients refused amputation in other hospitals before presenting to ours. This possibility notwithstanding, six patients still refused surgery in our hospital. This may reflect cultural perceptions or concerns about the resulting handicap or what patients consider the stigma of having only one leg. A few patients who refused amputation declared that they would rather die with their two legs than live with one leg. These observations underscore the need for thoughtful discussions with patients and family members when the need for amputation arises. There was also a high rate (53.1%) of above-knee and below-knee amputations in the present study as compared with the numbers reported from other series [11]. This could also reflect the late presentation of the patients to hospital. The lack of chiropodists and podiatrists in Saudi Arabia is also a serious limiting factor in the early detection, proper evaluation, and management of diabetic foot lesions.

The problem of diabetic foot disease, as seen in the populations of the Gulf states, deserves greater attention. The routine examination of the feet of all diabetic patients, either in the general clinic or a special diabetic foot clinic, is recommended so that high-risk cases can be detected early [12]. Every effort should be made to salvage the feet of diabetics with established lesions through proper foot rest, adequate antibiotic coverage, good control of diabetes, and debridement, as needed.

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FOLLOW-UP STUDY FOR MEASLES MATERNAL ANTIBODIES AND SEROCONVERSION AFTER MEASLES VACCINATION

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شملت هذه الدراسة ٧٢ طفلاً لتقصي أضداد الحصبة المكتسبة من الوالدة لدى أطفال تتراوح أعمارهم بين ستة شهور وتسعة شهور. شملت الدراسة أيضًا الانقلاب المصلي عقب إعطاء الجرعة الأولى من لقاح الحصبة في الشهر التاسع وتكرارها في الشهر الخامس عشر. كانت نتائج تقصي الأضداد سلبية في نسبة ٣٣٪ من الأطفال في الشهر السادس ونسبة ٣٦٪ في الشهر التاسع، مما يشير إلى استمرار إمكانية الإصابة بالحصبة. ولم يظهر فارق يذكر في مستوى الغلوبولين المناعي (ج) للحصبة بين الشهر السادس والتاسع من العمر. كانت نسبة الانقلاب المصلي عقب الجرعة الأولى من اللقاح في الشهر التاسع من العمر ٨٥٪، إلا أن الأطفال أظهروا زيادة واضحة في مستويات الغلوبولين المناعي (ج) للحصبة عقب اعادة التلقيح في الشهر الخامس عشر من العمر.

Seventy-two children were included in this study which examined measles maternal antibodies in children at the ages of six and nine months. The seroconversion after the first measles vaccination at nine months and revaccination at fifteen months was also evaluated. Results of testing were negative in 33% of the children at six months and in 36% at nine months, indicating continued susceptibility to measles. No significant difference was found in the measles IgG level between six and nine months of age. After the initial vaccination at nine months of age, the seroconversion rate was 85%. After revaccination at fifteen months of age, the children showed a significant increase in their measles IgG levels.

The persistence of maternal antibodies is the important cause of the primary vaccine failure observed in infants younger than twelve months [1-3]. The optimal age of vaccination remains controversial, and varies in different areas. Seroconversion studies in different populations can be done to determine the earliest age for effective vaccination [4]. Alternatively, a seroprevalence study can be carried out in young infants to determine when maternal antibodies are waning.

This study aims to evaluate measles maternal antibodies in children at six and nine months of age and their relationship to the mothers' measles antibody level in order to determine the earliest possible age of vaccination, the seroconversion rate after measles vaccination at the age of nine months, and the effect of revaccination at fifteen months of age.

Material and Methods

Seventy-two healthy children, who were referred from primary health care centers and who had normal growth parameters and no history of chronic illness at the age of six months, were included in the study. They were followed through four visits, and at each, a special form was filled out. The first visit was made at six months, and blood samples for measles antibodies were taken from the mother and child. At the second visit, when the infant was nine months old, additional blood samples were taken and the child vacci-

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Accepted for publication 24 March 1990.

nated (Schwartz vaccine; Rouvax Biomerieux). The third visit was scheduled when the child was fifteen months old. At that time a third blood sample was taken and an MMR vaccine given (Merck, Sharp, and Dohme). The fourth visit was scheduled two weeks following the MMR vaccination.

Twenty-one children had four samples taken. The vaccines were tested for potency using $TCID_{50}$ (tissue culture infective dose 50%). The end titer in Vero cells was determined using growth and maintenance media (Earl's minimal essential medium). The microtiter plate technique was used according to the manufacturer's recommendation (10^3 $TCID_{50}$ and over was considered usable). The measles IgG titer was measured with an indirect fluorescent technique using Virgo Electro Nucleonics Kits (USA); a reading of 1/8 and over was considered positive according to instructions of the manufacturer.

Statistical Method

The reciprocal values of fluorescent IgG titers were converted to a logarithm and examined using a paired *t* test [5]. The geometric mean of the titer (GMT) was computed to quantitatively compare the measles-specific antibodies at various ages. The outcome of vaccination at nine months was also expressed as a dilution rise between samples taken at six, nine, and fifteen months.

Results

Maternal measles antibodies determined at the age of six and nine months were negative in 20 of the 59 children (33.90%) tested at six months of age and in 17 of the 47 children (36.17%) tested at nine months of age.

The fluorescent measles IgG test was done at the first visit in 55 paired samples from the mothers and their children. A significant difference was found between the IgG titer of the mothers (GMT = 173.2) and the children (GMT = 7.2) ($P = 0.001$). No correlation was found.

Forty-four paired samples obtained from infants at the age of six and nine months were compared and the measles IgG level was not significantly different between the two ages (GMT = 6.1 and 5.3 at 6 and 9 months, respectively).

The measles IgG level was also compared in 35 paired samples obtained at nine months of age before vaccination and six months later. The GMT was 4.68 at nine months and showed a significant increase (36.76) at fifteen months ($P = 0.0001$). The correlation was 0.479 ($P = 0.002$).

In considering the seroconversion that took place after the initial vaccination at nine months, there was one or more dilution rise in 85.7% (30/35) of the children and a two or more dilution rise in 65.7% (23/35).

The IgG level was tested in 21 paired samples at fifteen months, before reimmunization (MMR vaccine), and two weeks later. The GMT was 28.98 before the second vaccination and increased significantly to 75 two weeks later ($P = 0.001$). The correlation was 0.556 ($P = 0.009$). Nineteen of the 21 children showed increased antibody titers after the MMR vaccination, and the remaining two showed the same titer.

Discussion

Almost one-third of the children were seronegative at 6 months of age. These children were thus susceptible to measles and required early vaccination. The lack of correlation between the measles IgG levels in the mothers and their children at this time can be explained by the different patterns of maternal antibody transfer and antibody half-life exhibited in different geographical areas [4,6].

The absence of a significant difference in the maternal measles antibody levels at 6 and 9 months of age supports vaccination at 6 months of age [7], taking into consideration that the large family size in our community is a contributing factor to the occurrence of measles in younger children.

The rising measles antibody titer after revaccination at fifteen months of age confirms its efficacy and that the initial early vaccination did not impair the protection induced by a second vaccine [8]. Our results agree with those reported for similar studies [5]. The significant difference between the measles antibody levels of mothers and children (even when reimmunized) may be due to a natural immunity acquired by the mothers and the lower antigenicity of the Schwartz vaccine [9]. The vaccine from the Edmonston-Zagreb strain seems to possess a higher immunogenicity, but the difference in the seroconversion rate is still not fully established [7].

Seroconversion following the initial vaccination at 9 months of age was 85.7% in terms of one dilution rise and 65.7% in terms of two. As the third blood sample was taken 6 months after vaccination at the age of 9 months, we consider one dilution rise as adequate proof of seroconversion. Our results are comparable to those found in other studies [10,11].

The persistence of maternal antibodies is the main cause of measles vaccine failures in infants younger than one year of age. Therefore, the vaccination should be delayed until the antibody levels wane. However, in a country such as Saudi Arabia where the measles immunization program has been only recently introduced and measles is still endemic [12], it is unwise to delay the vaccination. Hence it is preferable, at least for the present time, to continue vaccinating children below the age of one year, but with a compulsory booster dose six to nine months later. Conversely, as the seronegativity rate is high at nine months and the maternal antibody titers are not significantly different at six and nine months, it is preferable to administer the first dose earlier at six months to protect the susceptible children below nine months of age, who constitute almost one-third of the 6-month-old children in our study.

Promising results are expected from the new measles vaccines such as the Edmonston-Zagreb strain. Several studies have confirmed its higher immunogenicity. Provided this new strain will yield a higher seroconversion rate, it might be used as a single-dose vaccination administered at nine or even six months of age.

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THE IMMUNE STATUS OF YOUNG ADULTS TO RUBELLA VIRUS IN NORTHERN JORDAN

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تقصينا أضداد الحصبة الألمانية في عينات مصلية مأخوذة من ١٢٥٢ من اليافعين باستخدام اختبار إلايزا (ELISA) واختبار تثبيط التراص الدموي في محاولة لمعرفة الوضع المناعي للحصبة الألمانية لدى سكان شمال الأردن . كانت النسبة المئوية العامة لليافعين المعرضين ٢ ,٨٪ ولليافعات المعرضات ٦ ,٨٪ . ويعني ذلك أنه بالرغم من ارتفاع نسبة انتشار الأضداد المناوعة للحصبة الألمانية لدى جمهور اليافعات في الأردن إلا أن الخمج الطبيعي لا يوفر حماية كافية من الحصبة الألمانية على مايبدو. لذا، نوصي بوضع برنامج وطني لتلقيح اليافعات والبالغات من غير الحوامل واللاتي لن يحملن خلال ثلاثة أشهر من التلقيح إذا لم يسبق لهن أن تلقين لقاحًا للحصبة الألمانية ولم يشخص لديهن المرض بالفحص السريري . ومع أن درجة الترابط بين الاختبارين جيدة أظهر اختبار إلايزا (ELISA) حساسية أكبر من اختبار تثبيط التراص الدموي .

Serum samples from 1252 young adults were screened for rubella antibodies using an enzyme-linked immunosorbent assay (ELISA) method and hemagglutination inhibition test (HIT) in an attempt to establish the immune status for rubella among northern Jordanians. The overall percentage of susceptible adult males was 8.2%, while in females it was 8.6%. This implies that, in spite of the high prevalence of rubella-specific antibodies in the adult Jordanian female population, protection against rubella through natural infection appears inadequate. Therefore, it is recommended that a nationwide vaccination program be instituted for adolescent and adult females who are not pregnant and will not become pregnant within 3 months of vaccination, and who show no history of rubella vaccination or clinically diagnosed disease. The two techniques correlated well, though ELISA exhibited a higher sensitivity than did HIT.

Rubella is a benign self-limiting disease that usually occurs in childhood and is characterized by mild upper respiratory symptoms, preauricular lymphadenopathy, suboccipital lymphadenopathy, and an erythematous rash. Severe congenital anomalies, however, are seen in infants following maternal infection, especially those that occur in the first trimester [1,2].

Prevention of congenital rubella is the ultimate goal of any nationwide rubella immunization program. To reach this goal, two main immunization strategies have been applied in various countries [3–5]. They are direct protection through the vaccination of adolescent girls and adult women or indirect protection through vaccination of young children of both sexes. The national immunization program in Jordan currently covers measles, polio, whooping cough, tetanus, and diphtheria, but rubella and mumps are not included [6]. Despite the recommendation made in a preliminary report supporting the vaccination of young children of both sexes [7], based on hemagglutination inhibition test (HIT) findings, the exact need is still debated.

We report on the immune status of adults living

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Accepted for publication 17 March 1990.

in northern Jordan for rubella virus as determined using enzyme-linked immunosorbent assay (ELISA) and HIT methods. With this information we can address the need for a mass immunization program in the prevention of rubella infection during pregnancy.

Material and Methods

Blood samples were randomly collected from 660 male and 592 female, apparently healthy university students during the summer of 1987. Subject age ranged from 18 to 22 years and all were residents of northern Jordan; 51% came from urban areas and 42% from villages; 7% were Bedouins. Only 21 knew they had had childhood infection with rubella. Sera were separated and stored in aliquots at –20°C until further use.

In performing the HIT, rubella kits for the determination of IgG antibodies were used (Organon Teknika, F.R.G.). Tests were performed in V-shaped microsystem test plates. Nonspecific reactants were removed from sera using koalin suspension and absorption with chicken erythrocytes [8]. A titer of 8 or higher was regarded as positive and considered evidence of immunity.

ELISA kits using alkaline phosphatase (ELISA-AP; Lab System, Helsinki) were used. At the end of each run, the reaction was read at a wavelength of 405 nm using a Cecil digital ultraviolet spectrophotometer. Antibody levels of serum samples were expressed as enzyme immunoassay units (EIU), derived from known positive references. According to the manufacturer's instructions, EIU <10 was considered negative for IgG and EIU <20 was considered negative for IgM.

ELISA using horseradish peroxidase ELISA-HRP–conjugated sheep anti-human immunoglobulin was employed. At the end of each run, the reaction was read at a wavelength of 450 nm using a Dynatech Autoreader. Results were converted to international units per milliliter by means of calibration lines, using the provided low and high calibrators that correspond to 10 and 320 IU/ml, respectively.

To determine the extent of congenital rubella syndrome, a specially designed questionnaire was completed by six pediatricians and three gynecologists working in hospitals in northern Jordan. The information obtained reflected their observations during 1988 in newborns with evidence of congenital rubella syndrome (including cataracts, retinopathy, glaucoma, auditory defects, congenital heart defects, and mental retardation), and confirmed by laboratory methods (rubella IgM, ELISA-AP).

Results

Table 1 summarizes the prevalence of rubella antibodies in the sera examined, as detected by HIT and ELISA-HRP methods. HIT showed the highest titer of rubella antibodies was 1024 IU/ml and ELISA-HRP showed a value of 320 IU/ml. Differences based on sex or geographical distribution were not significant ($P > 0.05$).

Good correlation was found between both methods. All seronegative samples shown by ELISA-HRP were also negative on HIT, but not vice versa (i.e., 41 seronegative samples on HIT were positive on ELISA-HRP). Of the 146 sera yielding negative reactions on HIT or ELISA-HRP, 105 were negative with both tests. In addition, all seropositive samples on HIT were also positive on ELISA-HRP (Table 2).

TABLE 1. *Overall number and percentage of rubella seronegativity sample of young adults of both sexes in north Jordan, detected by HIT and ELISA-HRP.*

Sex	No. tested	HIT negative No.(%)	ELISA negative No.(%)
Male	660	72(10.9)	54(8.2)
Female	592	74(12.5)	51(8.6)
Both	1252	146(11.7)	105(8.4)

HIT = hemagglutination inhibition test; ELISA-HRP = enzyme-linked immunosorbent assay using horseradish peroxidase.

TABLE 2. *Correlation between the HIT method and ELISA-HRP method for the detection of rubella antibodies.*

	HIT-negative (No.)	HIT-positive (No.)	Total
ELISA-negative	105	0	105
ELISA-positive	41	1106	1147
Total	146	1106	1252

HIT = hemagglutination inhibition test; ELISA-HRP = enzyme-linked immunosorbent assay using horseradish peroxidase.

TABLE 3. *Description of 8 cases of congenital rubella syndrome in north Jordan during 1988.*

Patient No.	Time of symptom appearance*	IgM-ELISA-AP results (EIU)	CRS
1	2	53	Cataract
2	3	76	Cataract
3	2	85	Heart defect
4	1	62	Heart defect
5	2	71	Died after birth; heart defect
6	3	49	Died after birth; heart defect
7	2	86	Abortion
8	1	73	Abortion

*Month of gestation.
IgM-ELISA-AP = immunoglobulin M–enzyme-linked immunosorbent assay using alkaline phosphatase; CRS = congenital rubella syndrome; EIU = enzyme immunoassay units.

For further comparison, the 146 samples of both sexes that were negative on HIT with titers less than 8 were tested by ELISA-HRP and ELISA-AP. With both ELISA methods, a certain proportion of the samples were positive (ELISA-HRP, 15.3%; ELISA-AP, 13.7%). The potency of rubella antibodies of these samples varied from 10 to 160 IU/ml in ELISA-HRP and 10 to 60 EIU in ELISA-AP.

The results of the questionnaire revealed 20 cases of suspected congenital rubella syndrome among northern Jordanians during 1988, but only eight cases were confirmed by laboratory methods. Two children had cataracts; four had congenital heart defects (two of whom died after birth). Pregnancy was aborted in two women during the first trimester (Table 3).

Discussion

Congenital rubella syndrome is more frequently seen in developing countries where vaccination against rubella is not a common practice. However, the prevalence of rubella is not uniform throughout the world, and health authorities need to assess the incidence in their own countries or regions before deciding on the necessity of immunization. In Ethiopia and Egypt natural protection against the disease was found to be adequate, and a mass immunization program was not introduced for either young children or young adult females [9,10].

A preliminary survey conducted in northern Jordan and based on HIT findings [7] showed a 19.3% susceptibility to the rubella virus infection, whereas we found an 8.4% susceptibility. This difference may be due to the use of different assay systems and the size of the tested population sample. By using both HIT and ELISA, it was found that 88.3% of sera gave a positive reaction and 8.4% a negative reaction in both tests, indicating an overall correlation of 96.7% between the two methods. Only 41 samples were negative on HIT and positive on ELISA, yielding a discrepancy of 3.3%. In agreement with the observations of other investigators [1], ELISA was found to be more sensitive than HIT because a certain proportion of sera (13.7–15.3%), which were unequivocally negative on HIT, were found to contain rubella-specific antibodies on ELISA. In addition, ELISA proved to be a more precise, quantitative, and reproducible method.

The susceptibility of rubella among northern Jordanians (8.4%) is less than those reported for Morocco (29%) [11], Libya (25%) [12], Lebanon (15.6%) [13], and Bahrain (13.2%) [14], and more than those reported in Egypt (almost zero) [9], where widespread rubella epidemics do not occur. The percentage for Tunisia is almost the same as for Jordan (7%) [15]. It is therefore probable that, in Jordan, rubella occurs mainly as minor subclinical infections in adults, since only 21 of 1252 were aware of having had rubella infection.

Despite the high prevalence of rubella-specific antibodies in the adult Jordanian female population, protection against rubella by natural infection appears inadequate. However, if the susceptibility is 10%, the need for a routine vaccination is not urgent, and if 5%, the likelihood of congenital rubella being a public health problem is probably low [1]. Nationwide vaccination is recommended for adolescent and adult females who are not pregnant and will not become pregnant within three months of vaccination, and who have no history of rubella vaccination or clinically diagnosed disease. In support of this conclusion, an outbreak of rubella occurred in north Jordan at the time of this writing and hundreds of cases were reported.

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ACUTE APPENDICITIS COMPLICATING PREGNANCY

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يسبب حدوث التهاب الزائدة أثناء الحمل مشكلة صعبة لكل من الطبيب النسائي المعالج والجراح. قمنا باجراء دراسة مراجعة على ٥٢ مريضة تمت معاينتهن على التوالي خلال أربع سنوات في مستشفى الرياض المركزي، وهو من المستشفيات العامة الكبيرة والنشيطة. وقد تم تحليل الإصابة بالتهاب الزائدة في مراحل مختلفة من الحمل إضافة إلى الأعراض والعلامات الجسدية والنتائج المخبرية والمشاهدات الجراحية المتعلقة به. كما حللت المضاعفات المترتبة عليه وبخاصة وفيات الوالدات والأجنة وقورنت النتائج مع الدراسات المنشورة عن أماكن أخرى. لم يكن هناك أية وفيات للوالدات فيما بلغت نسبة وفيات الأجنة ٤٪. وتدل نتائج هذه الدراسة على أن بذل المساعي الحثيثة لتشخيص المرض ومعالجة المرضى جراحيًا من شأنه أن يقلل من معدل وفيات الوالدات والأجنة.

Appendicitis occurring during pregnancy presents a difficult problem for both the treating gynecologist and the surgeon. We studied retrospectively the cases of 52 consecutive patients seen during a four-year period at Riyadh Central Hospital, a large and busy general hospital. The incidence of appendicitis in various stages of pregnancy, along with its symptomatology, physical signs, laboratory results, and operative findings, were analyzed. The rates of complications, especially maternal and fetal mortality, were also analyzed and findings compared with those reported elsewhere. There was no maternal mortality and a 4% fetal mortality. We concluded that an aggressive approach in the diagnosis and surgical management of these patients reduces the maternal and fetal mortality.

Acute appendicitis developing during pregnancy poses a difficult management problem for both the surgeon and the gynecologist. Diagnosis of acute appendicitis is difficult because the symptoms may be attributed to the pregnancy, and physical findings may be obscured or altered by displacement of the appendix by the fetus. This can lead to delay in definitive treatment and hence the threat of fetal loss or maternal death, or both.

We retrospectively studied our 4-year experience (1405 to 1408 Hegira; August 1984 to August 1988) with cases of appendicitis occurring during pregnancy seen at Riyadh Central Hospital. This is one of the largest general hospitals in the Kingdom of Saudi Arabia, with a bed capacity of 1150.

The diagnostic problems, management, and complications are presented, along with a review of the medical literature.

Material and Methods

The records of 52 consecutive pregnant patients admitted between August 1984 to August 1988 (1405 to 1408 Hegira) with the clinical diagnosis of acute appendicitis on presentation were analyzed. All patients were seen by the gynecologist prior to surgery, who ruled out abortion. No pregnancy was found incidentally. Of these 52 patients,

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Accepted for publication 17 March 1990.

symptoms resolved quickly in six, and they were discharged home after investigation and observation. The remaining 46 patients underwent appendectomy and appendicitis was confirmed by both operative and histological findings.

Results

Riyadh Central Hospital serves a population of about one million. During the study period there was a total of 31,245 deliveries at Riyadh Maternity and Children's Hospital [1] (average, 10,000 per year). The incidence of acute appendicitis occurring during pregnancy at Riyadh Central Hospital was 1 per 680 deliveries. All appendectomies were performed by general surgeons.

Acute appendicitis was most common in the 15 to 25 year age group (N = 31, 68%), though the age range was 16 to 37 years (Table 1). It was most commonly seen in women during their second or third pregnancy (32 patients; 69%), though two patients were in their fifth pregnancy and one was in her seventh. Eighteen were primigravida, 14 were in their second pregancy, 12 were gravida 3 para 2, and five were gravida 4 para 3.

Acute appendicitis was less common in the later months of pregnancy. Twenty-two patients (48%) were in their first trimester, 20 (43%) in their second, and four (8%) in their third.

Symptoms and Signs

Forty-two patients (92%) had symptoms for less than 24 hours (range, 1 hour to 3 days). Forty-one patients (89%) were anorexic. Nausea and vomiting were common complaints and were seen in 25 patients (54%).

All patients complained of abdominal pain and had tenderness in the abdomen. Two patients showed tenderness in the right hypochondrium and both were more than 30 weeks' pregnant (Figure 1). Three patients had vaginal bleeding on presentation. One of them, who was 12 weeks pregnant, had incomplete abortion 10 days after appendectomy and had to undergo evacuation. The other with a gestational age of 11 weeks aborted within 12 hours after appendectomy, while the third patient who was six weeks pregnant had an uneventful recovery. Thirty-one patients (67%), all in their first and second trimester, showed tenderness toward the right side on rectal examination. Dysuria was infrequent (seven patients, 15%). Fever (greater than 37.2°C) was observed in 18 patients (39%). Alder's sign was positive in 35 (76%) patients while it was equivocal in the rest.

TABLE 1. *Breakdown of patients by age group.*

Age (yr)	Total No. of patients	No. of patients operated	Percentage
15–20	19	16	35
21–25	17	15	33
26–30	12	11	24
31–35	3	3	6
>35	1	1	2

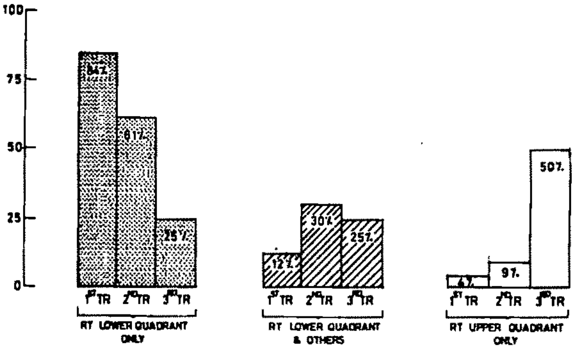

FIGURE 1. Location of abdominal pain in pregnant patients. Note the decreasing incidence of right lower quadrant pain and increasing incidence of right upper quadrant pain with advancing pregnancy. (*TR* = trimester).

Laboratory Results

A white cell count of up to 15.0 10^9/L is a normal finding during pregnancy [2]. In our series only 21 patients (47%) had leukocytosis of more than 15.0 10^9/L. Only seven patients (15%) had pus cells in their urine; two of these grew *Klebsiella pneumoniae* and one *E. coli.* One patient, who was 16 weeks pregnant, and whose cultures grew *K. pneumoniae*, had had two previous admissions for urinary tract infection during the pregnancy. This time her appendix was inflamed.

Twenty-eight patients (61%) underwent ultrasound examination of the abdomen prior to surgery and were found to have normal intrauterine pregnancy with normal adnexae and with some free fluid in the right iliac fossa. This was in addition to the pregnancy test which was used to confirm pregnancy in all patients.

Operative Management

All 46 patients who had appendectomy underwent the procedure within 12 hours after admission. Each patient received a general anesthetic and the operation was performed by a general surgeon with a gynecologist attending.

The location of incision varied: 30 (65%) had a muscle-splitting gridiron-McBurney incision, 12 (26%) had a Lanz skin crease muscle-splitting incision and three (7%) had a right paramedian incision, which was used because of a suspected perforated appendicitis.

Cephradine or cefotaxime (1 gm IV) was given as prophylaxis to all patients along with the premedication one hour before surgery. Antibiotics were continued for 48 hours at a dose of 1 gm IV six hourly if pus was found at operation or the appendix perforated.

Operative and Histological Findings

Only three patients had a perforated gangrenous appendix with pus in the right iliac fossa. The remaining 43 patients had acutely inflamed appendices, as proved by histological findings. Of the three patients with perforated appendices, two had had pain for two days and subsequently aborted.

Complications

Complications were minimal. There were two fetal losses but no maternal deaths. One patient who was 28 weeks pregnant went into premature labor postoperatively but the baby survived.

There were three wound infections (6.5%) encountered in the series. One patient aborted and one had premature labor, but both had perforated appendices. The third one had an inflamed appendix. *E. coli* and *Klebsiella* were grown from the wounds of the three patients, but the infections were subsequently treated successfully.

Duration of Hospitalization

The average hospital stay was 6 days, ranging from 5 to 12 days.

Discussion

Appendicitis is not more common during pregnancy [3,4]. Basically it exhibits the same pattern as in nonpregnant women but the diagnosis is more difficult in pregnancy because the appendix becomes shifted. After ectopic pregnancy, appendicitis is the next most common abdominal emergency seen during pregnancy, constituting 26% of such cases [5]. Our data show a higher incidence of appendicitis during the first and second trimesters. Other authors had similar findings [6–9], although contradictory reports exist [10,11].

Baer et al [12] demonstrated the variations in the position of the appendix caused by the enlarged uterus. The appendix lies at the iliac crest in the fifth month of the pregnancy and rises above that level during the last trimester [13]. This accounts for the pain and tenderness observed in the right upper quadrant and flank. Furthermore, the uterus lifts the peritoneum of the anterior abdominal wall away from the inflamed appendix, so that the clinical evidence of underlying peritonitis may be minimal and rectal examination findings equivocal.

Some tests can be helpful in establishing diagnosis (e.g., ballottement of the uterus from the left side may produce right-sided pain). Alders [13] described a sign that was very helpful in differentiating a uterine source of pain from an appendiceal source. The pain is localized when the patient lies supine. If then the patient is turned to the left, the pain shifts, then the pain is considered uterine or adnexal in origin. Appendicitis is suspected if the pain remains in the right iliac fossa. This is a useful and important clinical test and we use it routinely in every case.

The mortality of appendicitis complicating pregnancy is usually the result of delay in diagnosis and treatment [14]. Because of the possible absence of classic signs of appendicitis as seen in nonpregnant patients, diagnosis can lead to complications which may be fatal in the pregnant woman. The maternal mortality quoted in different series varies between 1% and 46% in the cases without perforation of appendix, rising to 35% at virtually all stages of gestation when perforation occurs [15]. In 1960, Black [10] published a review of 373 cases and found the mortality to be 0%, 4%, and 10% in each succeeding trimester. Hinshaw, in 1963, [16] found the mortality to be less than 2% in the first two trimesters, increasing to 16% in the third. O'Neill, in 1969, [2] found a maternal mortality of 1.5% in his series of 62 patients.

There was no maternal mortality in our series.

The fetal loss was 4%, in patients in both their eleventh and twelfth week of gestation who had had pain for more than two days. Black [10] reported an overall fetal mortality of 17%; Finch and Lee [17], 7.1%; Mohammed and Oxhorn [18] 20%; and McDonald [19], who published his report during the preantibiotic era, cited 37%.

We advocate the use of intraoperative antibiotics to reduce fetal mortality, with discontinuation after operation unless peritonitis or abscess arises.

We did not use progesterone and isoxsuprine to prevent premature labor, as has been used in some series [8].

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ENDOSCOPIC MANAGEMENT OF BILE DUCT STONES AT RIYADH MILITARY HOSPITAL: AN EIGHT-YEAR EXPERIENCE

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أجري مئتا تنظير باطني مع التصوير الراجع للمجاري الصفراوية والبنكرياس على مدى ثماني سنوات وذلك على مئة وواحد وستين مريضًا سعوديًا أدخلوا مستشفى القوات المسلحة بالرياض، المملكة العربية السعودية. أجري بضع المصرة اثناء التنظير الباطني لما نسبته ٩٣,٢٪ من أولئك المرضى ولم يجر ذلك للباقين الذين تمت احالتهم للعمليات الجراحية نتيجة لوجود الحصاة الصفراوية في كل من القناة الصفراوية الجامعة والمرارة. كانت الأعراض ظاهرة على كل المرضى، وكان من اكثرها تواردا المغص الصفراوي الذي شوهد في ما نسبته ٤٢,٢٪ من المرضى. وكان نسبة ١٤,٢٪ من المرضى أما يعانون من التهاب بنكرياسي حاد بحصاة الصفراء أو التهاب الأوعية الصفراوية وتلاشت تلك الآلام تماما بعد استخراج حصاة الصفراء. كانت عملية استخراج حصاة القناة الصفراوية الجامعة بالتنظير البطني ناجحة في ١٣٨ مريضًا (٨٥,٧٪)؛ في حين اخفقت في تسعة مرضى، وعولج ثلاثة منهم بتفتيت الحصى من خارج الجسم بالموجات الصدمية فنجح التفتيت في مريض واحد فقط. عانى ١٢ مريضًا من مضاعفات بضع المصرة واستخراج الحصاة بالتنظير، وكان أكثرها تواردًا النزف.

Over a period of eight years, 161 Saudi patients with biliary stones underwent 200 endoscopic retrograde cholangiopancreatographic studies at the Armed Forces Hospital, Riyadh, Saudi Arabia. Endoscopic sphincterotomy was performed in 93.2% of these patients and not attempted in the remainder who were referred for surgery because of biliary stones in both the common bile duct and gallbladder. All patients were symptomatic and the most common presenting symptom was biliary colic, seen in 42.2% of these patients. Either acute gallstone pancreatitis or cholangitis was seen in 14.2%, and this resolved completely following gallstone extraction. Endoscopic extraction of common bile duct stones was successful in 138 (85.7%) patients. Failure of stone extraction occurred in nine patients, three of whom received extracorporeal shockwave lithotripsy, which was successful in only one. Complications from endoscopic sphincterotomy and stone extractions occurred in 12 patients, of which bleeding was the most common.

Since the introduction of endoscopic sphincterotomy for biliary stone extraction in the early 1970s [1,2], there have been several reports on the successful extraction of biliary stones using this method [3,4]. Subsequently, endoscopic papillotomy has been used successfully in the treatment of disorders other than biliary stones. These include cholangitis and abscess drainage [5], pancreatitis [6], biliary parasite extraction, e.g., hydatid cyst [7], and ascaris removal [8].

We report our experience with 200 endoscopic retrograde cholangiopancreatographic studies (ERCP's) done in 161 Saudi patients with bile duct stones seen at Riyadh Armed Forces Hospital. This facility is a tertiary referral centre where, between June 1981 and June 1989, about 3530

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Accepted for publication 17 March 1990.

patients had cholelithiasis, of which 1664 had cholecystectomy.

Material and Methods

Between June 1981 and June 1989, 578 ERCPs were performed at the Riyadh Military Hospital, Riyadh, Saudi Arabia. Two hundred of these ERCPs were done in 161 patients with choledocholithiasis. Endoscopic sphincterotomy was performed in 150 of these patients for removal of stones from the common bile duct. Eighty-three of these patients had undergone previous cholecystectomy, 18 within two weeks of the sphincterot-omy, and these patients had a T-tube in situ. These patients were either referred from within the hospital or from other hospitals within the Kingdom. Patients were usually admitted but a few were treated as outpatients. Routine evaluation included full blood count, liver function tests, prothrombin time and partial thromboplastin time determinations, upper abdominal ultrasound, and other tests, if needed.

The method of endoscopic sphincterotomy has been described elsewhere [1,2]. It is performed in the endoscopy unit with the patient sedated using a side-view Olympus duodenoscope or video endoscope under fluoroscopic control.

Diagnostic ERCP is done first, and if there is a stone in the common bile duct, endoscopic sphincterotomy is performed with a diathermy wire. In cases where complete papillotome introduction is not possible, only a pre-cut is made which is usually enlarged on the next trial before final removal of stones.

Usually a Dormia basket is used to extract stones, but in a few instances, a balloon was also used (Figure 1). Small stones will usually pass spontaneously. If stones were extracted partially or could not be extracted, a second attempt was made after a few days. In patients with choledocholithiasis and dilatation of the common bile duct and in those with stones too large for immediate extraction, a nasobiliary drainage tube was usually inserted to achieve proper drainage. Mechanical lithotripsy was used to crush stones that were too large.

Patients with large stones in the common bile duct that could not be removed by endoscopic sphincterotomy were referred for surgery, especially if they had associated gallbladder stones.

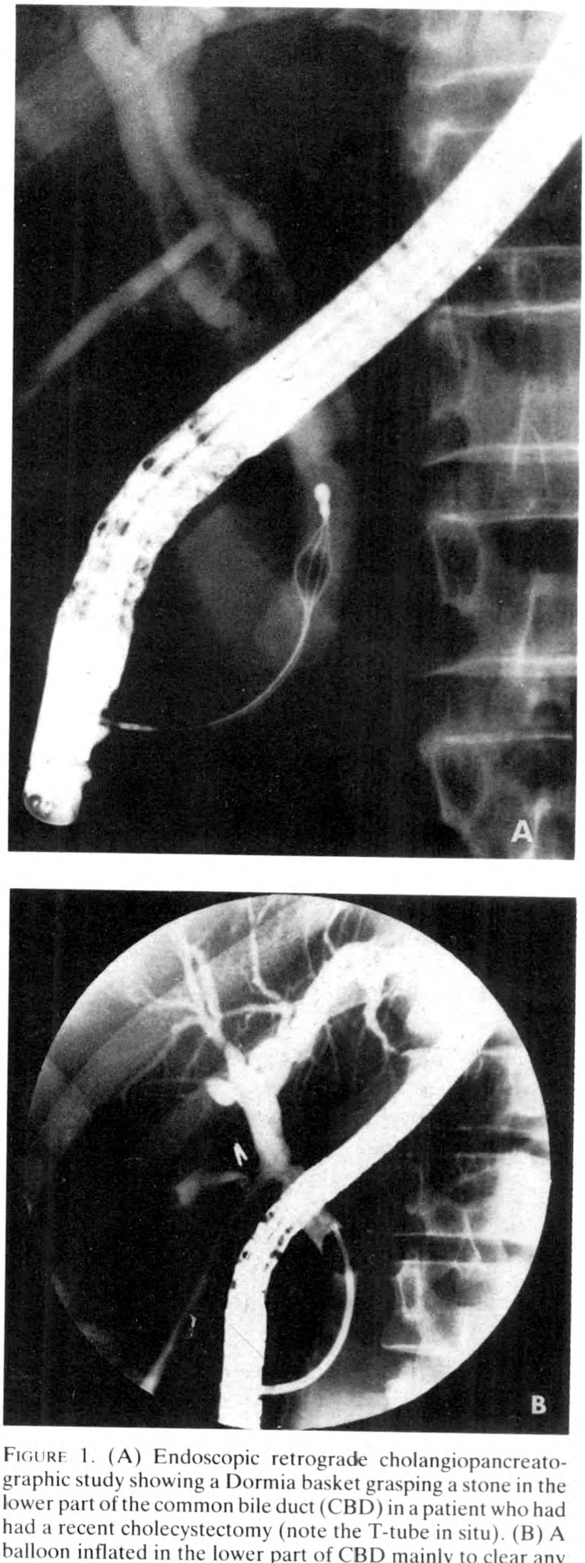

FIGURE 1. (A) Endoscopic retrograde cholangiopancreatographic study showing a Dormia basket grasping a stone in the lower part of the common bile duct (CBD) in a patient who had had a recent cholecystectomy (note the T-tube in situ). (B) A balloon inflated in the lower part of CBD mainly to clear any residual stones in a patient who had had cholecystectomy (note T-tube in situ).

Shockwave lithotripsy was also tried in those patients who were not good candidates for surgery because of severe cardiac or pulmonary disease.

Results

During the eight years under study, 161 patients with bile duct stones had 200 ERCPs, 39 of which represented second or third attempts. There were 98 males (age range, 23 to 70 years; mean, 42.5 years) and 63 females (age range, 25 to 80 years; mean, 38.0 years). Of these 161 patients, endoscopic sphincterotomy was done in 150 (93.2%). The remaining 11 patients were referred for surgery because of gallbladder stones in eight and stricture in the lower part of the common bile duct in three. A pre-cut was made in 12 patients that was enlarged in the second trial, followed by stone extraction.

Sphincterotomy was not done in two patients because both had had choledochoduodenostomy following previous surgery. One of these patients was found to have ascaris that was causing obstructive jaundice and intestinal obstruction.

The most common presentation was biliary colic, present in 42.2% of the 161 patients (Table 1). Fourteen had biliary pancreatitis, and all patients experienced improvement after endoscopic sphincterotomy and stone extraction. The pancreatic duct was visualized in 96 patients and abnormality was noted in three. A large amount of pus was released following endoscopic sphincterotomy in three patients who had cholangitis.

Table 2 summarizes the number, size, and site of the common bile duct stones. One patient had a large stone in the lower duct together with more than 50 small stones throughout the biliary tract (Figure 2). Seventeen patients had associated gallbladder stones and four intrahepatic stones; two of the patients had a history of ascaris infestation. One had ascaris removed from the common bile duct along with sludge, and had recurrent stones which were removed.

Because of impacted stone in the papilla and failed attempts at papillotome introduction, one patient underwent endoscopic choledochoduodenostomy using a needle knife, then the cut was enlarged using a sphincterotome, followed by stone extraction.

TABLE 1. *Main presentation in 161 patients.*

Presentation	No. of patients
Biliary colic	68 (42.2%)
Cholestasis	52 (32.3%)
Stone in T–tube cholangiogram	18 (11.2%)
Pancreatitis	14 (8.7%)
Cholangitis	9 (5.6%)

TABLE 2. *Characteristics of common bile duct stones.*

Characteristic	No. of patients
No. of stones	
1	78
2	28
3	14
4–7	38
10+	3
Size of stones (cm)	
0.5	63
0.5–1.0	46
1.0–1.5	38
1.5–2.5	10
2.5	4
Site of stones	
Upper CBD	39
Middle CBD	55
Lower CBD	67
Gallbladder + CBD	17
Intrahepatic CBD	4

CBD = common bile duct.

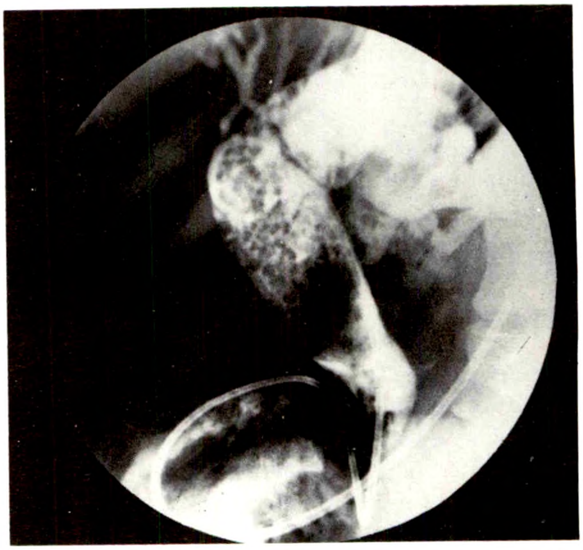

FIGURE 2. Endoscopic retrograde cholangiopancreatographic study showing a large stone in the lower part of the common bile duct with multiple small stones in the upper parts of the CBD and common hepatic duct. (Note nasobiliary tube inserted above the large stone, for drainage.)

Complete stone extraction was achieved in 138 patients (85.7%); three patients passed the stones spontaneously during follow-up ERCP. Residual stones remained in 20 patients (12.4%): endoscopic sphincterotomy was not attempted in 11 and stone extraction after endoscopic sphincterotomy failed in the remaining nine. All nine had single or multiple large common bile duct stones, but mechanical lithotripsy did not crush the stone in five. Six of the nine patients were referred for surgery while the remaining three underwent extracorporeal shockwave lithotripsy that was successful in only one patient.

Nasobiliary drainage was introduced in 38 patients (see Figure 2) and prophylactic antibiotics were administered in 22 patients following sphincterotomy. Complications from sphincterotomy occurred in 12 patients. Mild to moderate bleeding developed in eight patients and pancreatitis developed in four. These complications resolved with supportive treatment alone in all patients affected.

Discussion

Endoscopic sphincterotomy was a logical progression of ERCP, and is now the primary method of treating bile duct stones [9,10].

The main indication for endoscopic sphincterotomy is choledocholithiasis [3,9,10] following cholecystectomy, or in symptomatic patients with the gallbladder still in situ. More than 50% of our patients had had cholecystectomy, and biliary colic was the most common presentation in 42.2%.

Most series [3,9] report an 80 to 90% success rate for clearing the bile ducts of stones. The success rate in our patients was 85.7%, which falls within this range. Seventy-nine percent of the stones in our patients were extracted during the first trial. Nasobiliary drainage was introduced in patients with cholangitis and in most patients whose stones could not be removed at the first attempt. In these patients biliary drainage prevented stone impaction and further development of cholangitis [11].

Residual stones occurred in 20 of our patients; in nine extraction failed because the stones were larger than 2 cm in diameter. Extracorporeal shockwave lithotripsy was tried in three and was successful in one [12] and the other two patients were referred for surgery. In centers where shockwave lithotripsy is available, it is recommended in selected patients with both gallstones and common bile duct stones, with a high success rate [13].

Acute gallstone pancreatitis and cholangitis were the presentations in 14.2% of our patients. In both conditions, urgent papillotomy and stone removal are indicated [14]. All patients experienced improvement following papillotomy and stone removal. Early reports suggested that endoscopic sphincterotomy was superior to surgery in the treatment of acute gallstone pancreatitis [15], and this has subsequently been proved by controlled trials [6].

In developing countries, cases of recurrent stones and intrahepatic stones may be secondary to parasite infestation [16]. Two of our patients with recurrent stones had *Ascaris lumbricoides* [17]. In endemic areas, ascaris is as common as gallstones in the cause of symptomatic biliary and pancreatic disease. Pigment stones in the biliary tract can form on dead worms as the nidus, and stones related to ascaris are thought to form in the hepatic ducts and not the gallbladder [8].

Early complications of endoscopic sphincterotomy and subsequent stone extraction occur in 4 to 10% of the reported cases, hemorrhage being the most common [9,10,18]. Twelve of our patients (7.5%) had either bleeding or pancreatitis, but there were no deaths due to complications. The reported mortality rate of endoscopic sphincterotomy is about 1% [9,19], which is less than that reported for surgery, especially in the elderly, and for cases of reexploration for recurrent or retained common bile duct stones [20].

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HEMANGIOMA OF THE NASAL SEPTUM: A CLINICOPATHOLOGICAL PROFILE

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الوعاؤوم الدموي في حاجز الأنف سبب نادر للرعاف ولانسداد الأنف. تمت معاينة عشر حالات في مركزنا على مدى خمسة وعشرين عاما وتمثل هذه ٣١٪ من جميع حالات الوعاؤوم الدموي في الأنف. بلغت نسبة الذكور إلى الاناث ٢,٤ : ١، وتراوحت أعمار المرضى بين ١٤و٦٣ عاما (المتوسط، ٣٩ عامًا). كان العرض الرئيسي هو الرعاف مع انسداد أنفي مترقّ ووجدت قصة رضح سابق في ٧ حالات. تفاوتت مدة الأعراض من شهر ونصف الشهر إلى أربع سنوات (المتوسط، ١٣ شهرًا). كانت جميع الأورام، باستثناء واحد منها، تقع في الناحية الأمامية من الحاجز الأنفي، وتراوحت اقطارها بين ٠,٥ و٢سم. من الناحية النسيجية وصفت بأنهاأورام حميدة مغطاة بظهارة حرشفية مطبقة أظهرت درجات متفاوتة من التقرّح. كان اللب مكوّنا من تكاثر أوعية من النوع الشعري في ثماني حالات. بينما كانت الأوعية كهفية في حالتين. يعتبر التدخل الجراحي العلاج الأفضل في هذه الحالات، مع احتمال معاودة الورم في حالة عدم كفاية استئصاله (عاود الورم في حالتين من أصل عشر حالات).

Septal hemangioma is a rare cause of epistaxis and nasal obstruction. Ten cases were seen in our center over 25 years and constitute 31% of all cases of nasal hemangioma. The male to female ratio was 2.4:1; patient age ranged between 14 and 63 years (average, 39 years). The main presenting symptom was epistaxis with progressive nasal obstruction. There was a positive history of trauma in 7 cases. Symptoms varied between 1.5 months to 4 years (average, 13 months). All tumors but one were located anteriorly in the septum and measured between 0.5 and 2 cm in diameter. Histologically they were well-defined benign neoplasms covered with stratified squamous epithelium and showed varying degrees of ulceration. In eight cases the core was composed of proliferating capillary-type vessels, and two were cavernous. Operative intervention is the treatment of choice, with recurrences likely in the event of incomplete excision (two of the ten cases recurred).

Vascular tumors are the most common nonepithelial tumors arising in the nasal cavity, paranasal sinuses, and nasopharynx [1]. Hemangiomas represent only one class of benign vasoformative tumors that can involve the nasal cavity. Septal hemangiomas are, however, rare, and are an intriguing entity in that they present a diverse appearance and their treatment and pathogenesis are matters of some controversy. This paper attempts to establish septal hemangioma as a discrete clinical entity with well-defined histological correlates, and includes a review of the literature.

Material and Methods

The registry of surgical pathology at the American University of Beirut Medical Center was

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Accepted for publication 15 July 1990.

screened for cases of hemangioma seen over a period of 25 years. Thirty-two cases of nasal hemangioma were collected, not including cases involving the paranasal sinuses and nasopharynx. Ten cases had originated in the nasal septum and form the subject of this paper. Each patient's records were reviewed and data collected concerning symptomatology, potential causes, associated systemic findings, rhinoscopy findings, modes of treatment, and follow-up history. The histological preparations (i.e., glass slides stained with hematoxylin-eosin) were reviewed and the following characteristics noted: shape, stalk, external surface and structure, and type (i.e., capillary or cavernous). The criteria used for making histological diagnosis were those described elsewhere in the literature [2–4].

TABLE 1. *Septal hemangiomas: age and sex distribution.*

Patient No.	Sex	Age (y)*
1	M	14
2	M	17
3	M	25
4	F	29
5	M	34
6	M	48
7	M	48
8	M	54
9	F	55
10	F	63

*Average age, 39 years. M = males; F = females.

TABLE 2. *Septal hemangiomas: symptomatology.*

Patient No.	Epistaxis	Nasal obstruction	Rhinorrhea	Duration (mo)*
1	+	+	+	7.0
2	+	+	+	1.5
3	+	+	+	48.0
4	+	+	–	18.0
5	+	–	+	16.0
6	–	–	–	N.A.
7	+	–	+	24.0
8	+	+	–	1.5
9	–	+	–	3.0
10	+	–	–	2.0

*Average, 13 months. N.A. = not available.

TABLE 3. *Septal hemangiomas: history.*

Patient No.	Smoking	Trauma	Increase in size
1	+	Nose picking	+
2	+	Nose picking	+
3	–	—	+
4	+	—	+
5	+	—	+
6	+	Blunt	+
7	+	Blunt	+
8	+	Blunt	–
9	–	Cautery	+
10	+	Blunt	–

Results

Septal hemangiomas constituted 31% of the cases of intranasal hemangioma. Patient age ranged between 14 and 63 years (average, 39 years) (Table 1). There were seven males and three females (ratio, 2.4:1). Eight patients had a positive history of epistaxis (Table 2). In two, the bleeding was severe enough to necessitate frequent nasal packing. The rest had recurrent spotting produced by nasal manipulation. Unilateral nasal obstruction was present in six cases. It was partial initially but progressed to total obstruction in two patients, who also had the largest lesions. Unilateral nasal discharge, variously described as mucoid, mucopurulent, or blood-streaked, even foul-smelling, was the main complaint in five cases. Duration of symptoms varied between 1.5 to 48 months (average, 13 months) (Table 2).

Eight patients reported a gradual increase in the size of their nasal mass over periods varying between 2 months to 2 years (Table 3). Seven patients had a history of tobacco smoking. In another seven, there was a history of trauma caused by an external blunt injury to the nose or nose picking. One patient had undergone repeated electrocautery for epistaxis (Table 3).

Two patients were hypertensive and a third was diabetic and on oral hypoglycemics. None was receiving anticoagulants and none had hemangiomas elsewhere in the body. Anterior rhinoscopy findings on presentation consisted of a "reddish, soft, moveable mass" in three patients, a "dark nodular mass" in two, and an "easily bleeding ulcerated lesion" in five. Seven lesions were sessile and three (30%) pedunculated. The smallest was 0.5 cm and the largest 2 cm (Table 4).

Nine lesions were located on the anterior part of the septum in Little's area and only one was located posteriorly–superiorly in the nasal cavity at the junction of the cartilage with the perpendicular plate of the ethmoid. Seven were found in the left nasal cavity and three in the right. Lesions were all unilateral and single.

Local wide excision with a 2-mm margin of "normal mucosa," down to but not including the perichondrium, was performed in eight patients. The other two underwent limited excision (Table 5), but recurrence occurred after 6 weeks and 3 months, respectively. In both, the second lesion was smaller than the initial one. Wide local excision was then performed, but no further follow-up was available for either patient.

All ten hemangiomas were ovoid. All were lined externally with stratified squamous epithelium, which was keratinized in two cases and ulcerated in nine (Figure 1). The ulcerated surface involved 50 to 90% of the circumference of the lesion, and was accompanied by acute inflammation, granulation tissue, hemorrhage, and in one case, microbacterial colonization. Only one hemangioma had an intact surface.

Eight hemangiomas were the capillary type (see Figure 1). Their core was either lobulated or diffuse. The vessels had either prominent or inconspicuous lumina and were simple or branched. The endothelial cells were round to spindle-shaped.

Two hemangiomas had a cavernous pattern (Figure 2). The core of the lesion was formed of dilated spaces lined by flat endothelial cells. These spaces were congested and showed occasional adjacent areas of hemorrhage. The stalk was seen in only one case; it was lined by nasal-type epithelium.

One hemangioma could be construed as a pyogenic granuloma because it exhibited extensive ulceration and granulation tissue. Its basic architecture was, however, partially preserved.

One of the capillary hemangiomas partially resembled an hemangioendothelioma because of the proliferation of the endothelial cells.

TABLE 4. *Septal hemangiomas: anterior rhinoscopy.*

Patient No.	Location	Site	Size* (cm)	Appearance
1	L	Ant	1.0	S
2	L	Ant	1.0	P
3	L	Ant	2.0	S
4	R	Ant	1.0	P
5	R	Ant	0.5	S
6	L	Ant	1.0	S
7	R	Ant	0.8	S
8	L	Ant	0.5	S
9	L	Ant	1.5	S
10	L	Post Sup	0.5	P

L = left; R = right; Ant = anterior septum; Post Sup = posterior superior septum; S = sessile; P = pedunculated.
*Greatest dimension.

TABLE 5. *Septal hemangiomas: pathology, treatment, follow-up.*

Patient no.	Duration of symptoms (mo)	Size (cm)	Pathology	Treatment	Follow-up
1	7.0	1.0	CAP	Local wide excision	Cured
2	1.5	1.0	CAP	Local wide excision	Cured
3	48.0	2.0	CAP	Limited excision	Recurred
4	18.0	1.0	CAP	Limited excision	Recurred
5	16.0	0.5	CAP	Local wide excision	Cured
6	1.5	1.0	CAV	Local wide excision	Cured
7	24.0	0.8	CAV	Local wide excision	Cured
8	1.5	0.5	CAP	Local wide excision	Cured
9	3.0	1.5	CAP	Local wide excision	Cured
10	2.0	0.5	CAP	Local wide excision	Cured

CAP = capillary; CAV = cavernous.

Discussion

"Bleeding polyps" of the nasal septum were described more than ninety years ago by Pierce [5] and Schadewaldt [6]. "Polypoid hemangiomas" (Callison [7]) and "septal angiomas" (Dabney [8]) were other terms used to describe the same condition. "Bluetende septum polyp" (Schadewaldt [9]), "tumor sangrante benigno del tabique nasal" (Franchini [2]), and "emoangiome capillare del locus valsalvae" (Bordone [10]) were terms used in the European literature.

Around 183 cases of "hemangiomatous polyps"

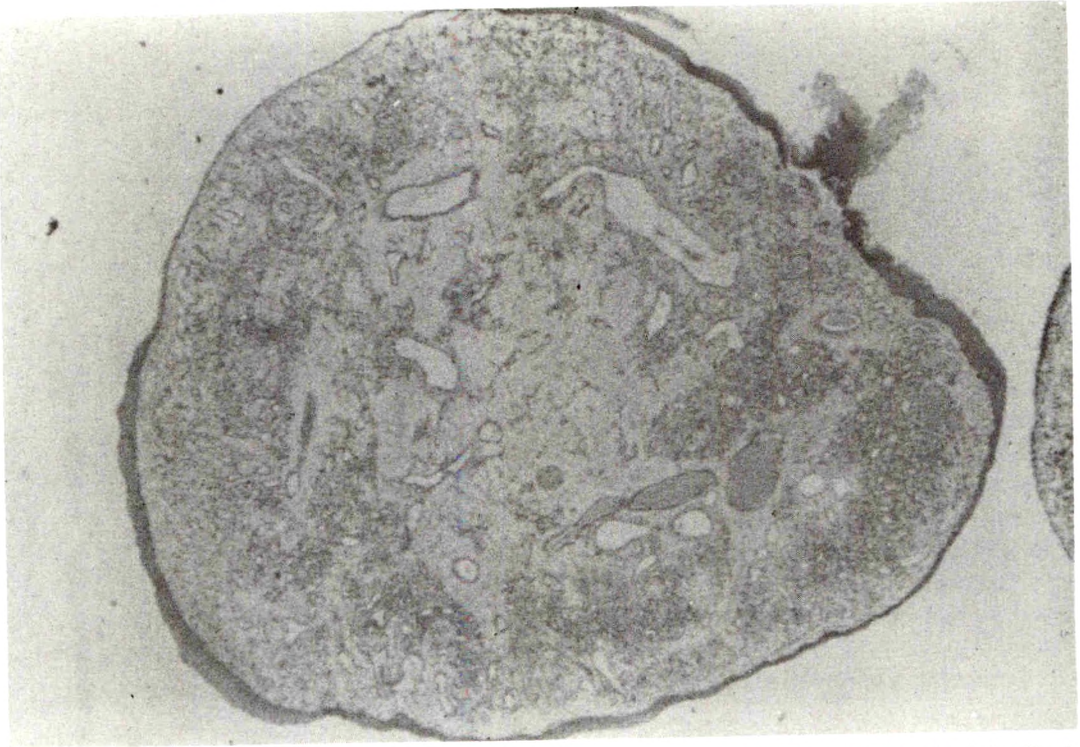

FIGURE 1. Septal hemangioma, capillary type. The hemangioma is covered by squamous epithelium that is focally ulcerated, with a typical lobular growth pattern of the new vessels. (H&E, original magnification, × 40.)

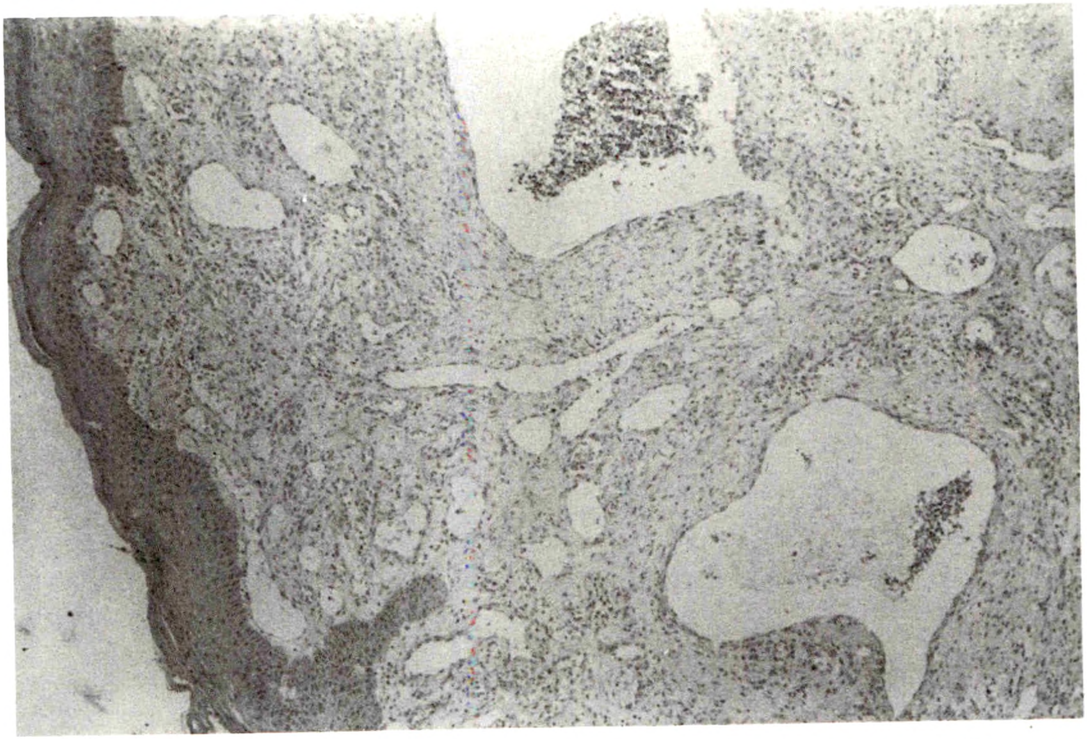

FIGURE 2. Septal hemangioma, cavernous type. These cavernous spaces are extremely congested. (H&E, original magnification, × 160.)

of the nasal septum were collected by Hasslauer [11], Pegler [12], and Goldman [13] in the world literature published until 1966. Osborn [14] reported on 32 cases in 1959, Ash and Old [15] on 23 cases in 1950, Fu and Perzin [1] on 19 cases in 1974, and Lineback [16] on nine cases in 1950. Most other reports have been of single cases.

Septal hemangiomas have usually been described in adults, rarely in children and adolescents. Pierce [5], Thomson and Negus [17], Lineback [16], Salvadori [4], and Goldman [13] reported on patients as young as 6, 5, 13, and 16 years, respectively. Five of the seven cases reported by Goldman [13] were in children. Earlier reports showed female predominance, but more recent reports have failed to substantiate this finding [13].

The anterior portion of the nasal septum facing the anterior third of the inferior turbinate is the most frequent site of involvement. The junction of the septal cartilage with the perpendicular plate of the ethmoid is the second most common site, followed by the vestibular area, the junction of the vomer and cartilage, and finally the floor of the nose [15]. The lesions are typically single and unilateral. Callison [7] reported on one patient with bilateral lesions.

The size of septal hemangiomas shown by anterior rhinoscopy varies between a few millimeters to 2.5 cm. Larger lesions are rare. Levey [18] reported one case of a black women who presented with a pulsatile septal mass that grew beyond the nares and infiltrated surrounding structures.

The growth in the nasal septum has variously been described as nodular, polypoid, mushroom-like, fleshy, highly vascular, easily bleeding, and even pulsatile [18]. It can be sessile or pedunculated and most reports describe gross superficial ulcerations.

Epistaxis is the most common presenting symptom, and is often severe. Rhinorrhea, a growing mass in the nose, and progressive unilateral nasal obstruction are common.

Theories concerning the pathogenesis of septal hemangiomas vary, pointing up the confusion as to their true nature. Havens and Lockhart [19] referred to "embryonic sequestrations of angioblasts present at birth." Smith and Pierce proposed the hormonal theory and reported, respectively, a case of septal hemangioma occuring during pregnancy [6] and a girl whose intranasal lesion bled during menses [5]. Osborn [14] theorized that "these angiomas are explained by the opening up of pre-existing non-patient channels." Trauma has also been incriminated as the cause for proliferation of blood vessels in the otherwise highly vascular Little's area [20].

All these theories remain speculative, but most authors agree that septal hemangiomas are acquired lesions that most probably represent benign neoplasms [1,4,14,15].

Several modalities have been proposed for the treatment of septal hemangiomas, including the use of sclerosing and freezing agents, electric cautery, cold snaring, and radiation therapy [16]. The recurrence rates with such modes of treatment have been high, however. Surgical excision is preferred by most authors. Mayer and Gluckman [6] stress the importance of excising a "cuff of underlying mucosa and perichondrium"; failure to do so increases the chances of recurrence.

Our observations have allowed us to draw some conclusions concerning septal hemangioma. It appears to be a benign neoplastic growth that most commonly involves the anterior portion of the septum. Trauma could play a leading role in its pathogenesis. We did not detect any congenital, hereditary, or hormonal factors in the etiology, and associated systemic findings were not significant.

Septal hemangiomas are also more frequently seen in males. Epistaxis, unilateral nasal obstruction, and rhinorrhea alone or in combination were the main presenting symptoms in all but one patient (No. 6) whose lesion was discovered during routine physical examination. The size of the lesion was related to the duration of symptoms; the largest lesion in our series (Patient 3, 2 cm) had been present for 4 years. Septal hemangiomas vary in their rate of growth but are generally slow growing.

A vascular growth with gross ulcerations is readily identified during physical examination. It tends to be sessile, single, unilateral, and more common in the left nasal cavity.

Histologically the capillary type predominates. Cavernous hemangiomas are much less frequent in the septum and tend to occur more on the turbinates. There is enough morphological evidence to consider a septal hemangioma as a vascular lesion. These lesions proliferate as a result of neoplastic, inflammatory, and traumatic causes, or can become telangiectatic and congested. Little's area contains a rich submucosal vascular network and is liable to trauma. It is thus not surprising to find hemangiomas in this location. Two of the lesions encountered in our series possessed features similar to a pyogenic granuloma and a hemangioendothelioma, but this finding does not confuse or lessen the diagnosis of a hemangioma since its basic structural characteristics are preserved.

Wide surgical excision with a margin of surrounding mucosa is the treatment of choice. The two cases of recurrences had been treated using only a limited local excision. It is this fact, exclusive of any other clinical or histological factor, that explains the recurrence.

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A COMPARATIVE STUDY OF DIFFERENT TREATMENTS OF HEMORRHOIDS

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تشكل البواسير مشكلة شرجية مألوفة في بلادنا وتعالج حاليًا بالعديد من الأساليب المختلفة. تم تقييم ثلاثة أساليب في تجربة عشوائية شملت ٨٤٨ مريضًا بالبواسير من الدرجة الثانية عولج منهم (٤٧٠) مريضًا بالجراحة القرِّية. تم تقييم مدى فعالية كل أسلوب علاجي من الناحية السريرية وذلك في الشهر الثالث، والسادس، والتاسع والثاني عشر بعد العلاج الأولي، استنادًا على مدى التحسن الذي طرأ على الأعراض التي قدموا بها. كان جميع المرضى يشكون من النزف المستقيمي وبروز الباسور عند التبرز، في حين أن نسبة ٦٩٪ منهم كانت تعاني من آلام شرجية و ١٤٪ من حكة شرجية. تبين أن أسلوب العلاج بالربط بالشريط المطاطي هو الأمثل مقارنة بالأساليب الأخرى وأظهر تفوقا احصائيًا بالنسبة للمعالجة التصليبية بالحقن والجراحة القَرِّية.

Hemorrhoid is a common anal problem in our country that is currently treated by many different methods. Three modalities were assessed in a randomized prospective trial in which 848 patients with a second-degree hemorrhoid were treated by rubber band ligation (470 patients), injection sclerotherapy (280 patients), or cryosurgery (98 patients). The effectiveness of each method was assessed clinically at 3, 6, 9, and 12 months after initial treatment, and determined by improvement in presenting symptoms. All patients complained of rectal bleeding and prolapse of the hemorrhoid on defecation, but only 69% had anal pain and 14% suffered from pruritus ani. Rubber band ligation was found to be superior to the other methods, and displayed statistical significance when compared to injection sclerotherapy and cryosurgery.

The true incidence of hemorrhoids is difficult to estimate. However, Goligher [1] suggested that at least 50% of the people older than age 50 have some degree of hemorrhoids that may or may not be symptomatic. The incidence in the Western Region of Saudi Arabia is quite high, as indicated by review of the medical records in our hospitals, which indicated that 10% or more of the surgical material seen in the outpatient department represented anorectal disorders: 90% of these were cases of hemorrhoids, 7% anal fissures, and 3% anal fistulae. An average of ten new cases of hemorrhoids are seen per week (520 cases per year).

Our experience in this country has revealed that the surgical treatment of hemorrhoids is either delayed, with patients undergoing prolonged conservative localized medical treatment and laxatives, or patients undergo unnecessary early surgery.

Many treatments are available, including hemorrhoidectomy, maximal anal dilatation, rubber band ligation, injection sclerotherapy, and cryosurgery. In this study we compared the effectiveness of the last three methods in the treatment of our patients with second-degree hemorrhoids.

Patients and Methods

This prospective clinical trial was carried out at

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Accepted for publication 18 December 1989.

King Fahd Hospital and Al-Shaty Hospital in Jeddah during January 1986 to December 1988. Eight hundred forty-eight patients with symptomatic second-degree hemorrhoids (bleeding piles with prolapse on defecation) made up the study population. Cases of third-degree and complicated piles and cases of hemorrhoids associated with anorectal disorders were excluded. The mean age, duration of symptoms, and nationality of the patients are summarized in Table 1.

Four hundred seventy patients were treated by rubber band ligation. The patient was placed in the left lateral position, without any prior preparation, and a single ligation applied at each visit. Three ligations were applied for each patient over two weeks. Another 280 patients were treated by injection sclerotherapy. This involved the submucosal injection of 3 ml of 5% phenol in almond oil into the pedicle of each pile at the level of the anorectal ring. The treatment was performed in one session. A further 98 patients were treated by cryosurgery. The patients were usually admitted the day before operation, and were given rectal enemas preoperatively. The procedure was performed with the patient under general anesthesia in the lithotomy position after simple anal dilatation. A liquid nitrogen probe (-89°C) (Frigitonics Down Surgical) was applied in the longitudinal axis of the internal piles, with the procedure taking an average of 15 to 20 seconds for each pile.

The three different methods were evaluated clinically in relation to the improvement in the presenting complaints. The patients were seen at 3, 6, 9, and 12 months after the initial treatment (Tables 2-4).

Results

On presentation all 848 patients complained of rectal bleeding and prolapse on defecation. Anal pain was also a complaint in 580 (68%) patients and pruritus ani in 118 (14%) patients. The results of the three different modalities are summarized below.

Rubber Band Ligation

Rubber band ligation was the treatment used in 470 patients (Table 2). Only 401 reported for the first follow-up at 3 months. At that time 41 still complained of rectal bleeding that occurred about

TABLE 1. *Mean age, symptom duration, sex, and nationality of 848 patients allocated to rubber band ligation, injection sclerotherapy, and cryosurgery treatment groups.*

Variables	Rubber band ligation	Injection sclerotherapy	Cryotherapy
No. of patients (N = 848)	470	280	98
Mean age (yr + SD)	36 ± 17	34 ± 13	35 ± 11
Duration of symptoms (mo ± SD)	50 ± 18	52 ± 19	49 ± 16
Sex (male: female)	270:200	160:120	50:48
Nationality (Saudi:non-Saudi)	230:240	180:100	60:38

TABLE 2. *Follow-up patients treated with rubber band ligation.*

Variables	Total no. of patients	Follow-up visits (mo) 3	6	9	12
Total no. attended	470	401	360	291	168
Rectal bleeding	470 (100%)	41 (10.2%)	27 (7.5%)	12 (4.1%)	7 (4.1%)
Prolapse on defecation	470 (100%)	29 (7.2%)	12 (3.3%)	8 (2.7%)	6 (3.6%)
Anal pain	311 (66%)	49 (12.2%)	11 (3%)	9 (3%)	3 (1.8%)
Pruritus ani	60 (12%)	18 (4.5%)	9 (2.5%)	6 (2%)	3 (1.8%)

Chi-square = 56.39; DF = 12; $P < 0.05$.

TABLE 3. *Follow-up patients treated with injection sclerotherapy.*

Variables	Total no. of patients	Follow-up visits (mo) 3	6	9	12
Total no. attended	280	246	249	180	92
Rectal bleeding	280 (100%)	43 (17%)	30 (12%)	22 (12.2%)	18 (19.5%)
Prolapse on defecation	280 (100%)	96 (36%)	49 (19.6%)	37 (20%)	31 (33.7%)
Anal pain	190 (67.8%)	39 (14.8%)	36 (14.5%)	31 (17.2%)	30 (32.6%)
Pruritus ani	41 (14.6%)	16 (6%)	14 (5.6%)	12 (6.6%)	11 (11.9%)

Chi-square = 23.48; DF = 12; $P < 0.05$.

TABLE 4. *Follow-up of patients treated with cryosurgery.*

Variables	Total no. of patients	Follow-up visits (mo)			
		3	6	9	12
Total no. attended	98	89	80	62	45
Rectal bleeding	98 (100%)	12 (13.5%)	9 (11.2%)	4 (6.4%)	4 (8.8%)
Prolapse on defecation	98 (100%)	--	--	2 (3.2%)	-- (4.4%)
Anal pain	69 (70.4%)	21 (23.6%)	5 (6.2%)	3 (4.8%)	3 (6.6%)
Pruritus ani	12 (12.2%)	8 (9%)	4 (5%)	1 (1.6%)	1 (2.2%)

Chi-square = 26.79; DF = 12; $P < 0.05$.

once weekly, but only when they were constipated; 29 of them noticed prolapse on defecation and 18 experienced itching after defecation. Proctoscopy revealed residual hemorrhoids and these required a further two to three ligations over two weeks.

A further 49 patients complained of anal pain or discomfort on defecation. Proctoscopy revealed congested submucosal veins with slight redness of the mucosa. Chronic constipation was a marked feature in all of these cases, and patients were given dietary advice to help regulate the bowel habit.

Three hundred sixty were seen at the 6-month follow-up. All 41 patients who had required religation attended. Fourteen were asymptomatic and 27 experienced occasional slight bleeding. Twelve of them continued to have rectal prolapse and nine still suffered from pruritus ani. Proctoscopy revealed one to two residual piles in these patients, treated by further ligation. Eleven patients still complained of anal pain or discomfort. Proctoscopy revealed obvious sphincter spasm along with congested mucosa. All were severely constipated. Dietary advice was given and a mild laxative prescribed.

Only 291 patients reported at 9-month follow-up. Of the 27 patients who experienced slight bleeding at 6 months, 26 were seen. Twelve complained of rectal bleeding and eight of these complained of prolapse on defecation. Six of the eight patients also complained of pruritus ani, which proctoscopy revealed was a residual hemorrhoid at 11 o'clock in all cases. Only nine patients still experienced anal pain. Proctoscopic examination revealed a congested mucosa with slight redness in these nine, and all were found to be either a consumer of spicy food or alcohol, which they were asked to avoid.

Only 168 patients reported for 12-month follow-up. Seven had minimal rectal bleeding that occurred on average once a month; six had prolapse and three of these had post-defecation itching. They were not inconvenienced by this and did not wish further treatment. Six still have anal pain on defecation that lasts for a half to one hour after defecation.

Injection Sclerotherapy

Only 264 patients reported for first follow-up at 3 months (Table 3). At that time, ninety-six patients complained of prolapse on defecation. Forty-three had rectal bleeding on average once a week; 36 had anal pain on defecation and 16 pruritus ani. Proctoscopy revealed persistent hemorrhoids in all 96 patients, and all underwent reinjection with 3 ml of 5% phenol into each pedicle.

Two hundred forty-nine patients were seen at 6-month follow-up. Only 86 of the 96 patients who underwent reinjection were seen; 49 still suffered prolapse on defecation, and of these 30 experienced rectal bleeding, 36 anal pain, and 14 pruritus ani. Residual hemorrhoids were found at proctoscopic examination. Regulation of the bowel habit was advised, and if necessary, suppositories with minimal cortisone content were ordered to relieve symptoms.

Only 180 patients reported at 9-month follow-up. Of the 49 patients with prolapse, only 37 reported and they had more or less the same complaints; these were 22 cases of bleeding, 31 of anal pain, and 12 of pruritus ani. Proctoscopy confirmed the presence of hemorrhids. No treatment was planned and further follow-up was advised.

Only 92 patients reported at 12-month follow-up. Thirty-one still had prolapse on defecation, 18 rectal bleeding, 30 anal pain on defecation, and 11 pruritus ani. These patients were subsequently treated by rubber band ligation.

Cryosurgery

Ninety-eight patients underwent cryosurgery for the treatment of their hemorrhoids (Table 4).

The average hospital stay in these patients was 2.75 days. The postoperative pain was managed with pentazocine (30 mg intramuscularly, 6 hourly prn) and the patients were followed up initially once a week because of disturbing serous discharge that occurred in 90.8% of the cases. This resolved within 2 weeks in all.

Discussion

The injection of carbolic acid as treatment for hemorrhoid was introduced by Mitchell in 1881 [2]. However, the complication rate was high and side effects severe because the injection was directed into the hemorrhoidal mass and this was followed by necrosis. The present method, using 5% phenol injected into the submucosa at the level of hemorrhoidal pedicles above the dentate line, Blanchard [3] claims was introduced by Albright in 1882. The technique was further improved by Gabriel [4] in 1963. Injection sclerotherapy became very popular in the U.K. and many reports continue to support its use. Greca et al [5] in 1981 concluded that injection sclerotherapy yielded results that were similar to those for rubber band ligation.

Other reports on injection sclerotherapy indicate disappointing results. Dencker et al [6] from Sweden reported in 1973 that only 21% of the patients were relieved of symptoms. Kilbourne [7], in his collective review of 62,910 patients published in 1934, reported a recurrence rate of 15% within three years. Milligan et al [8,9] found that further injections were required by 15%, 38%, and 69% of the patients with first-, second-, and third-degree hemorrhoids, respectively, but the late results of reinjection were not reported. Khoury et al [10] in 1985 indicated that reinjection will not improve results significantly. However, Beart [11] concluded that injection sclerotherapy is particularly well suited for patients with first-degree hemorrhoids who have minimal bleeding and discharge, but patients with second-degree hemorrhoids rarely obtained prolonged benefit.

The rubber band ligation was first introduced successfully by Blaisdell [12] in 1958 for the prevention of massive hemorrhage secondary to hemorrhoidectomy. Barron [13] in 1963 developed his own instrument (Barron's ligator) and applied it for the treatment of internal hemorrhoids with astonishingly good results. This modality has been quickly accepted worldwide because it is cost effective, safe, and simple to apply and is well tolerated by patients. The good clinical results increase the popularity of rubber band ligation [14] in the treatment of first-, second-, and even third-degree hemorrhoids, though with different results for each. Many comparative studies and trials have been performed to prove its efficiency. Murie et al [15] in 1981 demonstrated the effect of hemorrhoidectomy on anal pain, discomfort, pruritus ani, and fecal soiling, which was similar to that of rubber band ligation. Murie et al [16] in 1982 reported that (for follow-up periods of from a few months to one year) rubber band ligation was almost as effective as hemorrhoidectomy and somewhat more effective than injection sclerotherapy. Williams and Crapp [17] in 1975 could not demonstrate a significant difference between the effects of rubber band ligation and cryotherapy, and Hood and Williams [18] in 1971 showed that maximal anal dilatation yielded results similar to those for rubber band ligation. Murie et al [16,19] in 1982 demonstrated, over a 3-year follow-up period, that rubber band ligation produced lasting results in the relief of rectal bleeding, hemorrhoidal prolapse, anal pain, pruritus ani, and fecal soiling. He therefore recommended rubber band ligation as first line treatment for prolapsing hemorrhoids. The study showed results at one year that were identical to those found at 2 and 3 years. Other reviews [20-22] indicated that 70% of the patients were cured after banding, but Jeffrey et al [23] in 1980 noted residual symptoms in 69% of their patients, while Corman [24] in 1984 indicated the effectiveness of the further rubber band ligation in the treatment of residual symptoms. However, patient discomfort has been noted to increase with an increase in the number of ligations in each session. Groves et al [25] performed a single ligation at each session. Stern et al [26] in 1987 advised against inserting more than two ligations at each session, at 3 to 4 weeks apart. Other authors [27,28] claimed that three ligations were tolerated by their patients. In our trial we applied single ligations at weekly intervals and those were well tolerated by our patients.

Despite poor cooperation in our patients at attending follow-up, rubber band ligation was

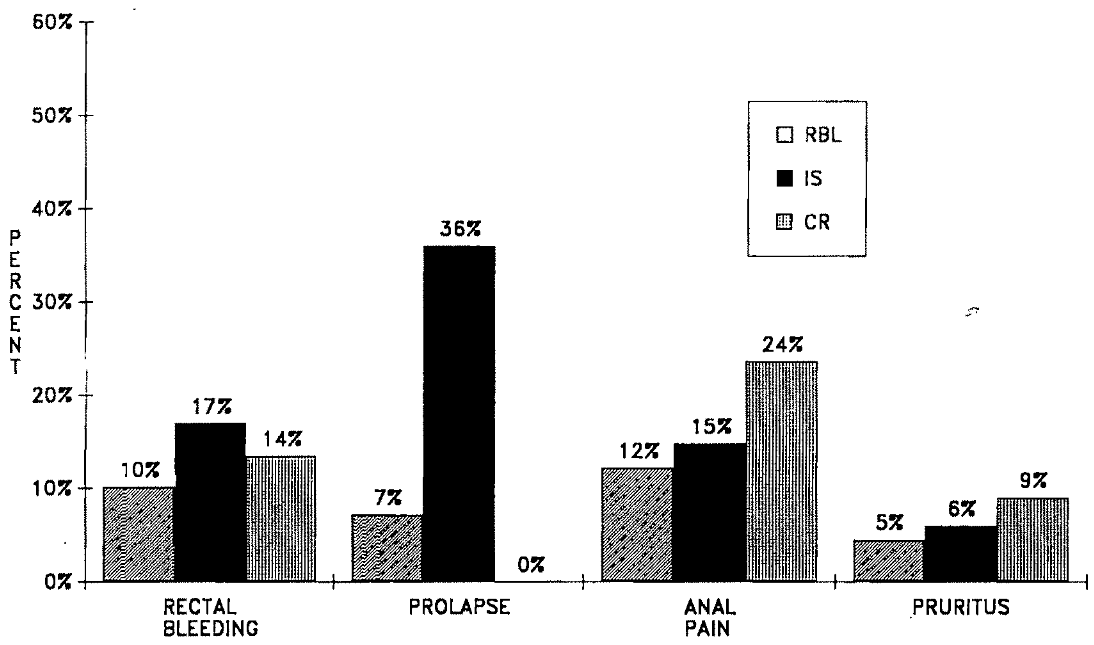

FIGURE 1. Comparison of symptoms in patients 3 months after treatment. (*RBL* = rubber band ligation; *IS* = injection sclerotherapy; *CR* = cryotherapy.)

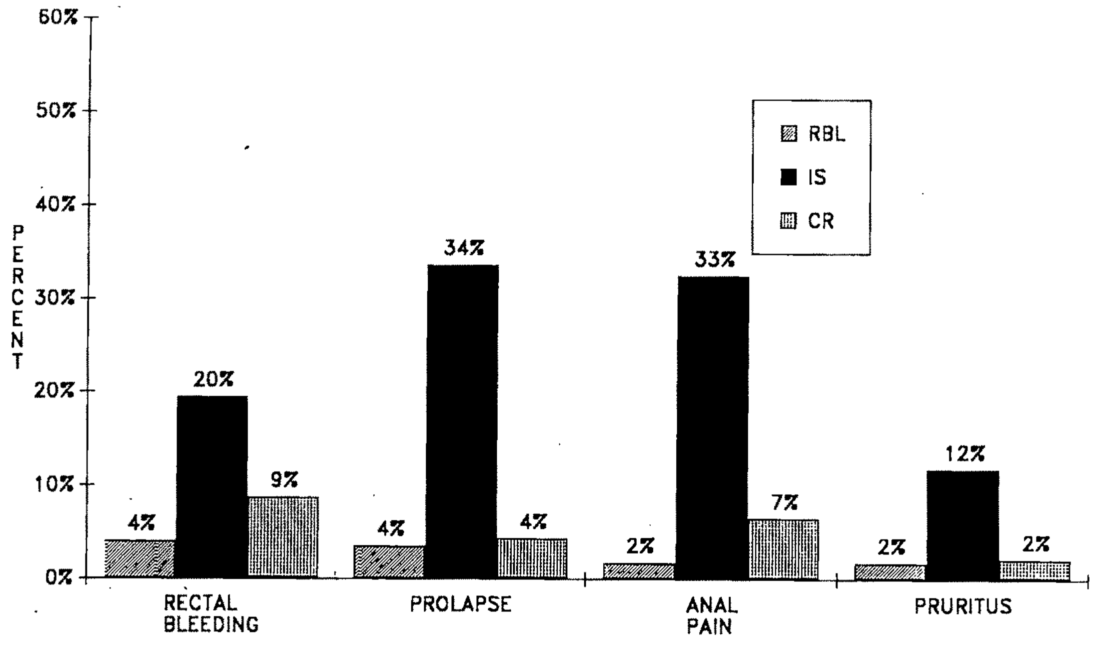

FIGURE 2. Comparison of symptoms in patients 12 months after treatment. (*RBL* = rubber band ligation; *IS* = injection sclerotherapy; *CR* = cryotherapy.)

observed to achieve better overall results at the various follow-up intervals than did either injection sclerotherapy or cryosurgery. The 10% failure rate in our trial was due to technical difficulty in ligating the hemorrhoids at the correct level, particularly at 11 o'clock, and the fact that three ligations are not adequate to completely cure some patients' hemorrhoids. Therefore, to achieve a higher percentage of cure and to minimize recurrence, four to six ligations are advisable. Depending on the degree of hemorrhoids, severity of symptoms, and the size of the hemorrhoidal masses, patients with residual symptoms can have further ligations.

Cryotherapy should only be performed in certain selected cases, because it requires hospital admission, general anesthesia, and the administration of postoperative analgesics for at least one week. The postoperative course in 90.8% of our patients was marred by serous discharge. This problem was also reported by O'Connor [29]. Wilson and Schofield [30] and Savin [31] also reported an increased incidence of serous discharge and prolonged recovery for such patients. Smith et al [32] reported a study in which both closed hemorrhoidectomy and cryotherapy were performed in 26 patients. Although pain was initially less after cryotherapy, 12 patients experienced prolonged pain on the side of the cryotherapy compared to three patients who had pain on the resected side. Patients were able to distinguish which side had been resected and which had been frozen. Of 24 patients examined one year later, 13 had residual hemorrhoids, 12 on the cryosurgical side.

Our experience with cryosurgery shows that taking into consideration the experience of the aforementioned authors, if the rubber band ligation does not give satisfactory results, the treatment should be shifted to operative hemorrhoidectomy rather than cryosurgery.

Eight-nine patients attended 3-month follow-up. At that time, 21 complained of anal pain at defecation; 12 of them reported minimal rectal bleeding and eight of these also had pruritus ani. Proctoscopy revealed congested mucosa and incomplete healing at the edges of the area of cryosurgery.

Only 80 patients were seen at 6-month follow-up. Nine still complained of minimal rectal bleeding once a week; five of these experienced anal pain at defecation which required analgesics, and four of them also had pruritus ani. Proctoscopy revealed no organic pathological findings, except sphincter spasm.

Sixty-two were seen at 9-month follow-up. Four complained of minimal rectal bleeding if severely constipated; two of them had partial prolapse of one hemorrhoid, three of them had anal pain, and only one had pruritus ani. On proctoscopic examination, residual hemorrhoids were seen at either 11 or 3 o'clock and all were treated by rubber band ligation.

Comparison of the results of the three different methods at 3 and 12 months is shown in Figures 1 and 2. The superiority of rubber band ligation over the other two methods is clearly evident.

Similarly, statistical analysis using the chi-square test indicated the superiority of rubber band ligation (×56.39) over injection sclerotherapy (×23.48) and cryosurgery (×26.79) (Tables 1-3).

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DEPRESSION OF PHAGOCYTIC ACTIVITY OF THE IMMUNE SYSTEM FOLLOWING TRADITIONAL CAUTERY IN EXPERIMENTAL ANIMALS

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يمارس الكي التقليدي على نطاق واسع في المملكة العربية السعودية وبعض الأقطار الأخرى ولكنه لم يتعرض حتى الآن لاستقصاء علمي دقيق. لذا، قيمنا تأثير الكي على جهاز المناعة غير النوعي لدى حيوان طبيعي في محاولة لايضاح بعض تأثيراته الفيزيولوجية. تم كي ذكور جرذان (ويستر) وخنازير غينيا بصورة تشابه الكي التقليدي في الحجم والنسبة المئوية للمنطقة المكويّة. قيمّنا تأثير الكي على جهاز البلعميات وحيدة النواة في الجرذان باستخدام قبط وتصفية محلول غرواني للكبريت المشع. قيست هبّة الفعالية التنفسية في الكريات البيض مفصصة النوى المحيطية لدى الخنازير الغينية بعد الكي باستخدام أسلوب اللمعان الكيميائي، وأظهرت النتائج هبوطا ملحوظا في تصفية الغرواني داخل الأوعية مع ازدياد زمن التصفية بعد الكي. وبالاضافة إلى ذلك، هبط قبط الكبد للغرواني في الحيوانات المكوية بالمقارنة مع حيوانات مجموعة الضبط، وتناقص عدد الكريات البيض أيضًا بدرجة هامة. كما أظهرت الدراسة تثبيطا ملحوظا في وظيفة البلعميات لدى الخنازير الغينية في الدم الكامل وفي الكريات البيض مفصصة النوى المحيطية المعزولة. وتدل هذه النتائج على أن الكي التقليدي يسبب هبوط الوظيفة الفيزيولوجية لجهاز البلعميات في حيوانات التجربة الطبيعية. أما تأثير الكي التقليدي على الحيوانات المخموجة فإنه يستحق مزيدا من الاستقصاء.

Traditional cautery, which is practiced widely in Saudi Arabia and some other countries, has not been exposed to detailed scientific investigation. In an attempt to elucidate some of its physiological aspects, we assessed the effect of cautery on a normal animal's nonspecific immune system. Male Wistar rats and guinea pigs were cauterized to simulate traditional cautery in size and percentage of cauterized area. Using radioactive sulfur colloid uptake and clearance, the effect of cautery on the mononuclear phagocyte system was evaluated in rats. The respiratory burst in peripheral polymorphonuclear leukocytes (PMNs) after cautery was measured in the guinea pigs using the chemiluminescence technique. The results showed marked reduction in the intravascular clearance of the colloid with prolonged clearance time following cautery. In addition, the liver uptake of the colloid was reduced in cauterized animals compared with control animals and the white cell count was also significantly reduced. The study showed marked inhibition of phagocytic function in guinea pigs in both whole blood and isolated PMNs. These results indicate that traditional cautery reduces the physiological function of the phagocytic system in normal experimental animals. The influence of traditional cautery on infected animals deserves further investigation.

Traditional medicine is practiced widely in various countries in keeping with social and cultural traditions. To promote such traditional self-reliance, the World Health Organization established programs to effect the incorporation of useful traditional practices into the general health care delivery system of such countries by the year 1989. At

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Accepted for publication 27 March 1990.

least two centers for research on traditional medicine will have been identified in each region [1].

Cautery, which consists of treatment by thermal injury or heat, is one of the most common methods used by traditional healers in Saudi Arabia, and is used in the treatment of a wide variety of disorders including disk prolapse, gastroenteritis in children, pneumonia and pleurisy, facial palsy, and some mental or psychological problems. Although there are some differences in the methods used by various healers, there is general agreement on the size and site of cautery for specific problems; for example, for disk prolapse all healers perform it with a circular shaped iron rod applied around the lateral malleolus.

We are unaware of a study that examines the mechanism by which cautery cures or relieves symptoms of disease. However, as some of the conditions for which cautery is commonly used are infectious or inflammatory, it is possible that cautery may affect the body's defense mechanisms. The aim of this study, which was done on experimental animals, was to assess the effect of traditional cautery on the nonspecific immune system (i.e., the phagocyte system).

Material and Methods

Experimental Animals

Male Wistar rats were used as the experimental animals to evaluate the influence of traditional cautery on the mononuclear phagocyte system (MPS) function, as determined by sulfur colloid uptake and clearance. The peripheral polymorphonuclear leukocyte respiratory burst after cautery was measured in guinea pigs using a chemiluminescence technique [2–4]. The two different sets of animals were selected on the basis of technical reasons only. Both animal species were obtained from the Animal House, College of Medicine, King Saud University, Riyadh. Table 1 summarizes the experimental design.

TABLE 1. *Experimental design for assessing MPS function in rats and guinea pigs.*

Item	Study I (3 spots)	Study II (1 spot)
Cautery area	1.7%	0.58%
Rats:		
Phagocytosis	99m Tc-S colloid clearance rate	99m Tc-S colloid clearance rate
MPS organ distribution	99m Tc-S colloid uptake by liver, spleen, kidneys, and lungs	99m Tc-S colloid uptake by liver, spleen, kidneys, and lungs
White blood cell & differential count	0, 6, 12 days	
Days	0, 2, 6, 12 days	0, 2, 6, 12 days
Number of animals used	5 per group	5 per group
Guinea pigs:		
Chemiluminescence	Whole blood and PMNs	Not done
Days	0, 6, 12 days	Not done
Number of animals	5 per group	

MPS = mononuclear phagocyte system; 99m Tc-S = technetium 99m–labeled sulfur; PMN = polymorphonuclear leukocytes.

Cauterization

The size of the cautery surface area is important, as in burned animals when more than 15% of surface area is involved there is marked inhibition of phagocytosis [5–8]. Thus the size of the cautery area was kept minimal to conform with the common practice of the traditional healers. The average diameter is about 0.2 cm. Two sizes were used: 1 point (0.2 cm) and 3 points (3 × 0.2 cm). The back of the animal's neck was shaved and the animal anesthetized with ether. Once the animal was under deep and complete anesthesia and no longer responded to painful stimulation, a metal rod (diameter, 0.2 cm) was heated on a Bunsen burner until it glowed red (Figure 1). This was then applied for 3 seconds to the selected site on the animal. This method is similar to that used by traditional healers, although they do not use anesthesia or painkillers. The percentage of the cauterized area was calculated as follows: Percentage of cauterized area = a/b × 100, where *a* is the surface area and *b* is the total surface area for rats, which is approximately 0.07 m^2. Phagocytic function was determined by the intravascular clearance rate of colloid, tissue distribution, white blood cell count (WBC), and chemiluminescence peak response. The radiolabeled sulfur colloid was prepared according to the method described by Larson and Nelp [9] and Saad et al [10].

Determination of MPS Phagocytic Function

Male Wistar rats weighing 300 to 500 g were used. These rats were anesthetized with ether

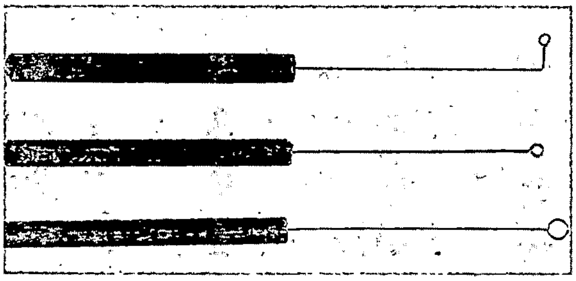

FIGURE 1. Samples of rods commonly used for cauterization by traditional healers.

prior to injection of the colloid. A 23-gauge butterfly cannula was inserted via the tail vein. The upper thigh was then exposed through a detector and the other parts of the body covered by lead. This detector was attached to the two-channel scintillation detector interface. The rate of clearance of colloid was then read every 30 seconds for 20 minutes at 10-second counts. All readings were plotted using logarithmic paper.

The distribution of the labeled colloid was also measured in the individual MPS organs. Total percentages of activity in the body taken up by each organ were calculated [9,10].

Assessment of Phagocyte Respiratory Burst

To study the influence of traditional cautery on peripheral phagocytes, whole blood or isolated polymorphonuclear leukocytes (PMNs) were obtained from cauterized guinea pigs before cautery, and at 2, 6 and 12 days thereafter. The phagocyte respiratory burst activity was monitored in vitro by lumino-dependent chemiluminescence [2–4]. Venous blood samples were obtained from cauterized as well as noncauterized guinea pigs. Heparin was used as an anticoagulant (10 U/ml). PMNs were isolated as described by Al Tuwaijri et al [11]. The PMNs were then diluted in phosphate-buffered saline to a concentration of 5×10^6 cells/ml. Cell viability was tested by trypan blue (0.2% W/V) exclusion.

Chemiluminescence Assay

A Luminometer (LKB-Wallac 125) with a constant-temperature (37°C) sample holder was used for measurement of chemiluminescence. It records the light emission (in millivolts) on a digital display which is well correlated with the amount of oxygen produced from phagocyte cells and ultimately the degree of phagocytosis. This allows us to examine precisely the phagocytic activity in vitro even in whole blood, using a small quantity of blood (100 μl). Phorbol myristate acetate was used as a soluble phagocyte stimulus.

Statistical Analysis

All values were expressed as the mean ± standard error. Student's *t* test was used to assess the differences between the measurements at different time points of cauterization. The results were considered significant at $P < 0.05$.

Results

The influence of cautery on the general health of both rats and guinea pigs was minimal with no mortality, and the thermal burns healed within 7 to 10 days following cautery. The average size of the cautery was 0.58% of the total surface area in the group of animals receiving one-spot cauterization and 1.7% in the three-spot group. There was no change in the animals' body weight, or in the weight of the liver, spleen, or lungs.

The cauterized rats showed a marked reduction in the intravascular clearance of colloid. Both the slow and fast clearance rates were significantly reduced ($P < 0.01$) compared with those in the control group (Table 2, Figure 2). The cauterized rats showed a significantly prolonged clearance time in the fast rate compared with that in the control group ($P < 0.05$). Similarly, the intravascular clearance slow rate was tremendously prolonged in cauterized animals compared with that in the control group (Figure 2, Table 2). The rate of clearance was markedly reduced in all cauterized rats regardless of the time intervals following cautery.

The ability of MPS organs (liver, spleen, lungs, and kidneys) to take up radioactive colloid, as an indicator of phagocytic activity in cauterized animals, was markedly changed following cautery. The percentage of 99m Tc–sulfur colloid in the liver was significantly reduced compared with that in control animals at 2, 6, and 12 days following cautery. In the other organs, colloid uptake was either increased (lungs) or not markedly affected (spleen) (Table 3).

The results also showed that there was no significantly different effect on MPS function associated with the two sizes of cautery area used (0.58 or 1.7% of the total body surface area).

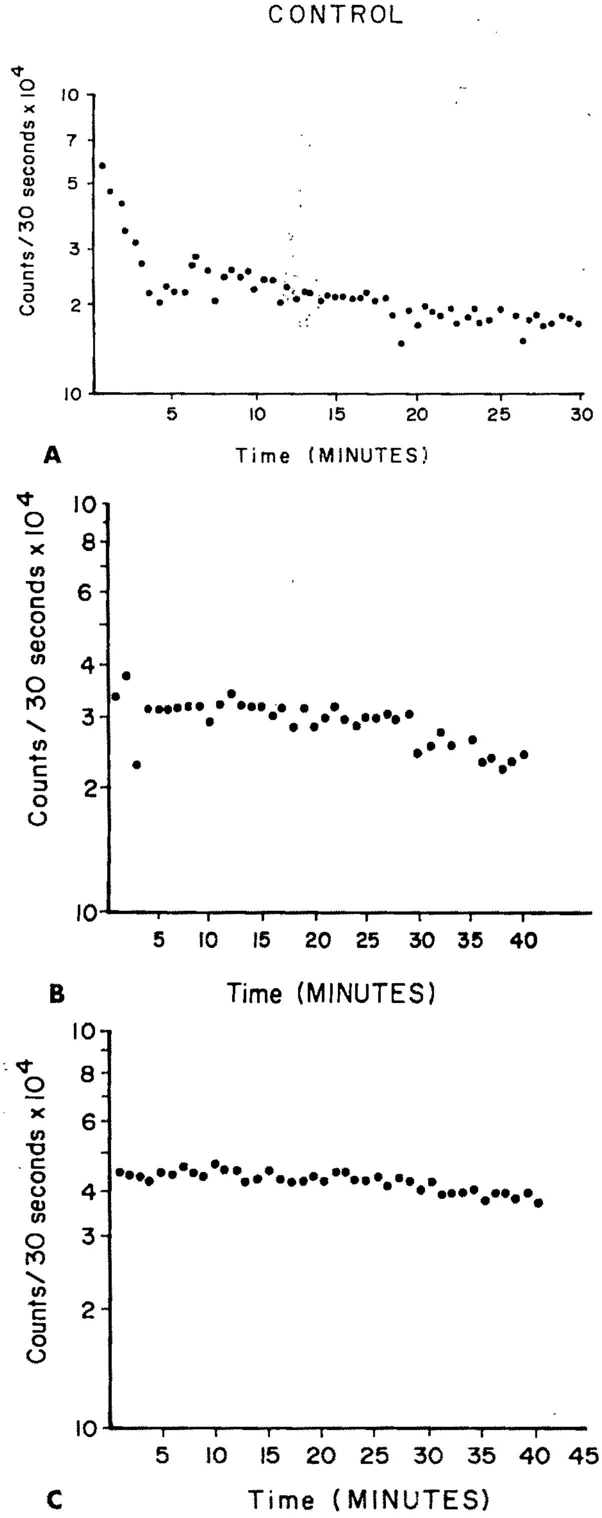

FIGURE 2. A biexponential plot of 99m T-sulfur colloid intravascular clearance in (A) control rats, (B) cauterized rats at 6 days post cautery, and (C) at 12 days post cautery.

TABLE 2. *Influence of traditional injury on phagocyte function measured by 99m Tc-sulfur colloid intravascular clearance in rats.*

Group	Intravascular clearance rate (min)		
	Days	Fast rate	Slow rate
Control	0	4.7 ± 1.2	29.7 ± 1.8
Cautery	6	27.3 ± 8.5*	63.3 ± 2.4†
Cautery	12	39.0 ± 13.0§	106.5 ± 21.5¶

All values are expressed as the mean ± S.E. 0.5 ml of 99m Tc-sulfur colloid was injected via the tail vein; three spots of cauterization were done at 6 and 12 days prior to injection of the colloid.
* $P < 0.003$; † $P < 0.001$; § $P < 0.05$; ¶ $P < 0.03$.

TABLE 3. *Percentage uptake of 99m Tc-sulfur colloid distribution in the mononuclear phagocyte system organs of male Wistar rats.*

Study group	Liver	Lungs	Spleen	Kidneys
Control	81.12 ± 1.2	5.36 ± 0.65	4.86 ± 0.72	8.62 ± 0.66
Cauterized				
Day 2	56.10 ± 5.2*	23.00 ± 3.9*	5.29 ± 1.33	15.48 ± 4.1
Day 6	67.00 ± 5.0	17.50 ± 2.5*	3.00 ± 1.0	12.50 ± 1.5
Day 12	76.34 ± 1.4†	8.36 ± 0.9†	3.63 ± 0.8	11.56 ± 1.1

All values are expressed as the mean ± S.E. 0.5 ml of 99 m Tc-sulfur colloid was injected in the tall vein. Three spots of cauterization were done 2, 6, and 12 days prior to injection of the colloid.
* $P < 0.01$; † $P < 0.05$.

In rats, the total WBC count was significantly reduced at 2, 6, and 12 days after cautery in cauterized groups compared with that in control animals (Table 4). A similar reduction was found in the values of neutrophils, lymphocytes, and monocytes in the differential count.

There was a significant inhibition of phagocytic function of both whole blood and isolated PMNs in cauterized guinea pigs, as measured by chemiluminescence, compared with that in control animals.

The maximum peak response of PMNs measured by chemiluminescence was markedly reduced to 63.6 and 8.8 mV in cauterized animals at 6 and 12 days, respectively, following cautery, compared with 68.7 mV in control animals (Figure 3, Table 5). The same pattern of inhibition was shown using whole blood, although the response was relatively lower.

Discussion

In the last few decades, depression of experi-

TABLE 4. *Influence of traditional cautery on total and differential white blood cell and differential counts in guinea pigs at different time intervals post cautery.*

Group	Day	Total white blood cells	Neutrophils	Lymphocytes	Monocytes	Eosinophils
Control	0	8200 ± 240	1370 ± 88.56	6625 ± 80.36	180 ± 13.94	82 ± 0.00
Cauterized	2	6200 ± 230	880 ± 140.12	5189 ± 121.52*	111 ± 30.38	124 ± 62.00
Cauterized	6	5800 ± 230*	713 ± 75.98*	4910 ± 63.22*	127 ± 31.32	116 ± 0.00
Cauterized	12	5900 ± 460*	649 ± 102.07*	5115 ± 70.80*	100 ± 32.20*	59 ± 0.00

All values are expressed as the mean ± S.E. Cauterization was done 2, 6, and 12 days prior to measurements. Cautery was done in three locations.
* $P < 0.01$.

TABLE 5. *Phagocytic function of whole blood and PMNs of normal and cauterized guinea pigs stimulated with PMA at different time intervals post cautery and measured by chemiluminescence.*

Group	Whole blood		PMNs	
	Max. peak (mV)	Integral (mV/min)	Max. peak (mV)	Integral (mV/min)
Control	5.96	40.47	68.70	567.9
Day 6	1.89	8.98	63.58	77.88
Day 12	1.18*	2.02*	8.80*	89.29*

PMNs count: 5×10^6 ml.
Incubation temperature: 37°C. Cauterization was done in three locations. Chemiluminescence was measured at 0, 6, and 12 days post cautery. Phorbol myristate acetate concentrate was 10^{-5}M and luminal concentrate was 10^{-4}M.
* $P < 0.001$.
PMN = polymorphonuclear leukocytes.

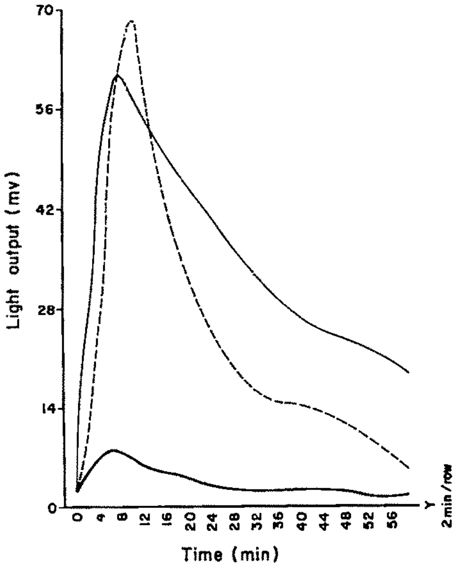

FIGURE 3. Chemiluminescence profile of polymorphonuclear leukocytes obtained from normal guinea pigs *(heavy solid black line)*, and at 6 days *(broken line)* and 12 days *(thin solid black line)* after cauterization.

mental animal host defense system following thermal injury (burn) has been widely reported [12–15]. Several experimental studies have shown that the activity of the hepatic phagocytic cell of the MPS is markedly inhibited after thermal injury and circulatory shock [5,16–19] and increases the animal's susceptibility to infection and reduces microorganism clearance by the MPS in animals infected with bacteria [6,12]. Another study found a selective depression of the peritoneal macrophage function in burned mice [20]. The mechanism by which thermal injury induces the MPS depression has not been clarified. Several questions remain, including why is there a marked depression in the MPS after thermal injury? More specifically, what is the factor (or factors) responsible for the inhibition of the MPS following thermal injury? Also, which steps of the phagocytic process are altered?

Thermal injury was shown to reduce the clearance of erythrocyte debris, and was also found to be associated with a depression of MPS phagocyte function. Loegering et al [21–23] have studied the possibility that hemolysis following thermal injury plays the key role in this process.

Moreover, studies have demonstrated that experimental thermal injury induces a depressed intravascular clearance rate of test particles that bind to undefined receptors on hepatic macrophages [8,14,22]. In vitro, thermal injury has also been observed to reduce the phagocytosis of yeast particles by alveolar and peritoneal macrophages [7]. Recently, Cuddy et al [15], who studied the effect of thermal injury on complement receptors in vivo, found a significant depression in the in vivo clearance function of hepatic complement receptors following thermal injury. This reduction may contribute to the susceptibility to infection associated with thermal injury. Lastly, a profound inhibition of LTB4 and oxygen release in PMNs was noted in patients who suffered total body surface area burns of 40 to 80% [24].

Several points can be drawn based on the findings of these earlier studies. First, a correlation exists between the severity of thermal injury and the degree of impairment of MPS. Second, all the earlier findings, whether obtained from experimental animals or human studies, were obtained in cases of a relatively high percentage of burn injury (more than 15%) of total body surface area. Third, there are no studies in which thermal injury was applied to a small surface area (1 to 2%).

In the Kingdom of Saudi Arabia, a large number of Arabic traditional healers practice traditional cautery in large cities, villages, and the desert. Patients with a wide variety of diseases resort to this type of treatment, especially if modern treatments fail. These native Arabic healers believe that traditional cautery is a nonspecific treatment for a broad spectrum of diseases, both organic and nonorganic. They apply cautery to treat bacterial infections such as pneumonia and viral infections such as viral hepatitis. Traditional cautery is also used to treat neurological diseases, and may be supplemented by medicinal plants and herbs.

The size of the traditional thermal cautery area (percentage of burned skin) varies, depending on the practitioner, but is usually less than 2% of the total body surface area. The average sizes we have seen in cauterized patients were between 1 to 2 cm in diameter. The number and sites of cautery marks also vary depending on the location of pain. The traditional healers believe in a specific site for a specific disease.

The results of the present study indicate that traditional thermal injury (cautery), although usually involving a small area, causes significant depression of MPS phagocytosis in normal experimental animals. This is indicated by the depressed blood clearance capability of the hepatic phagocytic cells of the MPS. The concentration of radioactive labeled colloid in the liver, the major port of the MPS, is significantly reduced. This finding agrees with those in earlier reports [6,8,13,17,25,26]. Conversely, Ikeuchi et al [27] reported activated macrophages in the spleens of burned mice, and Guo and Gu [28] showed that peritoneal macrophages are activated in the early period after the burn, then they begin to be depressed thereafter.

In contrast to previous studies in which there was more extensive thermal injury (26–28%), the thermal injury (cautery) inflicted in our study was minimal (less than 2% of the total body surface area). The size of thermal injury may play an important role in a diseased host, especially if he or she suffers from an infection. Since this study was conducted on healthy experimental animals, one cannot conclude that the minimal thermal injury (less than 2% of the total body surface area) inhibits disease. However, the traditional cautery we performed in normal rats caused a depression in the MPS phagocytic capacity and inability to clear the foreign particles from the blood stream.

In addition, using chemiluminescence, a marked inhibition of respiratory burst function was observed in the neutrophils of animals subjected to thermal injury. Total WBC and differential count were also significantly altered after thermal injury. Interestingly, endocytosis in hepatic macrophages, represented by a fast clearance rate, was markedly depressed in cauterized compared with noncauterized rats. The slow phase of the blood intravascular clearance rate of colloid was also reduced, yielding a prolonged half life in cauterized animals compared with normals.

Acknowledgment

We acknowledge the support and funding for this work given by King Abdulaziz City for Science and Technology.

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Special Communication

WHAT MAKES OSCE A GOOD ADJUNCT TO THE CONVENTIONAL METHODS OF ASSESSING CLINICAL COMPETENCE?

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Learning assessment is a formidable task facing all educators. The problem is not a recent one, but dates back as far as 4,000 years to China when the first record of such an assessment has been found [1]. The challenge of finding the perfect tool for assessment is especially difficult when this tool must fully and accurately measure all aspects of the three domains in a field as complex as medicine. The cognitive domain can be satisfactorily assessed using the written format, namely the objective (e.g., MCQ) and essay questions, but the psychomotor and affective domains remain difficult to assess.

Faced with the challenge of assessing clinical competence, educators have applied various methods in an attempt to find the most accurate tool, including written, oral, and short and long practical cases. All, however, have proved to be deficient or defective in meeting the three most important criteria: validity, reliability, and practicality [2–5].

Because of the various drawbacks of these instruments, an innovative approach for assessing clinical competence was introduced in 1975 [2]. The Objective Structured Clinical Examination (OSCE), or better named OSCA (with the *A* for assessment) [6], is an instrument for clinical assessment that has shown a promising ability to determine validity, reliability, and practicality. In this evaluation, examinees rotate through a series of stations at brief intervals of a few minutes each. At each station, some predetermined specific aspect of a clinical encounter is assessed. Real or simulated patients may be used. Some stations may be in written (e.g., MCQ) or other (e.g., x-ray studies) format. The examinee is rated using a standardized checklist. The raters may be the physicians, specially trained non-physician health professionals (e.g., nurses), or patients, who act both as examination subjects and raters.

In this short report, the literature will be reviewed regarding the most important features of the OSCE, namely: validity, reliability, practicality, acceptability by all participants, and feedback feasibility.

Validity

A valid test is one that measures what it is supposed to measure [3,4]. Validity has been divided into content validity, construct validity, and criteria-related validity. The last category has been subdivided into concurrent validity and predictive validity [4]. The OSCE has been described as a valid tool for assessing clinical competence. This description takes into account history-taking, physical examination, identifying patient problems, identifying the appropriate investigation and interpreting the results, and recommending and undertaking appropriate management action [3]. Content and construct validity were found to be high [4,7]. In a questionnaire survey, 92.5% and 95% of the students felt the written and practical components, respectively, had high to moderate relevance to the content area of the tested subject. In the same study, the construct validity was inferred from the respectively higher scores of examinees who took the same test at different levels of training [4]. A different group of investigators found the predictive validity was high [8].

Reliability

Reliability mainly relates to the objectivity of

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Accepted for publication 20 June 1990.

assessment and the accuracy of the results [3]. The most important variables of a practical clinical examination are the examinees, the patients, and the examiners. In the OSCE the patient and examiner variables are better controlled [3].

The general reliability of OSCE has been well documented [2–7,9–12], and is mainly due to the use of standardized checklists to assess predetermined standards of clinical competence. Using statistical computations, the interstation projected reliability was found to increase as the number of stations increased. This form of reliability was also proved to increase as a function of testing time, with 6 hours for a 15-station test being optimal. This mainly applies to the MCQ theory test, short answer test, and static stations [5]. The interrater reliability was not found to be a source of major bias [5,12].

Practicality

The practicality of OSCE was suggested by its founder [3,10], and takes into account several factors: the number of students to be examined, the number of available staff and their specialties, patient availability, space and accommodation, and the use to be made of the results (e.g., pass or fail).

In institutions where a large number of students have to be tested, OSCE can serve this purpose adequately in a relatively short period. The number of students tested has ranged from 60 students in one day [5] to 110 students in one morning [3]. Others have tested 229 students in two mornings [13]. Using more than one set of similar stations allows for the assessment of even larger numbers of candidates [10].

This economic use of time can be counterbalanced by the lengthy preparation time [2,3,9,11,13,14]. However, with better planning and the use of an OSCE data bank, the time required for preparation can be shortened appreciably [3,9,14].

Exposure to certain areas, such as gynecology, for many examinees can be a major practical limiting factor. However, this was not found to be a difficulty but instead the financial cost of the test was a problem, as every patient was given $50 [15].

The cost of this practical assessment was found to be comparable to that of NBME test part 2. The latter costs $15 per student, while the equivalent OSCE cost was $21 per student for a 17-station test. Increasing the reliability of the OSCE to 0.8 can increase the cost to $65 per examinee. If the same reliability of 0.8 is to be reached using long case examinations, $200 per examinee is required [7].

Acceptability

Undoubtedly any newly introduced method of assessment will receive a mixed reaction, especially from examiners and examinees.

On the average, examiners' reactions to OSCE have been positive [9,13]. It particularly orients them to the practical weaknesses of the students [9,15,16]. It is well perceived by most examiners as an objective assessment of student performance [9,15].

In general, students have found the OSCE to be a very acceptable method of assessment [10,11,14]. The main reasons for this have been that the OSCE makes them appreciate the importance of clinical skills [9,15]; they also derive appreciable feedback [15,16] and it is both objective and fair [9,13,15]. It is viewed as being less stressful than conventional examinations [13] and the stress diminishes as the examination proceeds [15]. It also has the advantage of placing examinees in direct contact with their clinical supervisors [16].

Examination of the patient by many students may be unacceptable, especially if the area to be examined is sensitive, as in gynecological examinations. However, this was found not to be the case by both real and simulated patients, who, to the contrary, found it an enjoyable experience [15].

Feedback

Though not an essential part of an assessment tool, the feasibility of a test that provides feedback is of utmost importance. The importance of the feedback is greater if the instrument is used for formative rather than summative assessment. One of the cardinal features of the OSCE is its effectiveness in providing immediate feedback to both students [2,3,10,11,14,15,17] and staff [2,3,10,11].

Students prefer to get the feedback during the examination rather than afterward. Giving students their marked checklist and having them view a videotape which shows the standard answer to the item tested is preferred. This method was more acceptable to students than was either the checklist plus videotape provided after the examination or the checklist plus peer performance given during the examination [17]. The feedback was not associated with undue stress and was well provided with minimal extra input from the staff.

It is obvious from this brief literature review that the OSCE possesses several important features. In none of the practical conventional assessment methods does one find as many features combined into a single assessment tool. The OSCE does, however, have disadvantages.

The OSCE, which is the most objective practical means to assess clinical competence so far devised, shares a cardinal characteristic with the objective written examinations (e.g., MCQ) in that both make multiple biopsies of the area to be assessed [5]. This is a major drawback since competency in carrying out a specific clinical skill as assessed by the OSCE does not necessarily reflect the ability to take care of the patient as a whole [2,3,10]. This problem can be overcome by combining the OSCE with other forms of clinical assessment.

In OSCE, as in other methods of clinical examinations using human subjects, the competencies related to emergency situations cannot be well incorporated. The affective domain remains only partially assessed, at best, by the OSCE. Assessment of this domain requires more frequent, almost continuous, formative assessment than do other domains. Due to lack of better alternatives and an abundance of worse ones, it is clear that the OSCE should be used to assess clinical competence. It may not suffice as the sole method of assessment, but will be useful as an adjunct to conventional methods of clinical assessment.

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NONTRAUMATIC CEREBROSPINAL FLUID RHINORRHEA: REPORT OF TWO CASES AND REVIEW OF LITERATURE

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Cerebrospinal fluid (CSF) rhinorrhea or otorrhea is a distinct clinical condition that has been classified by Ommaya et al [1] into two broad etiological groups: traumatic and nontraumatic (NT) leaks. The former is a much more common condition, while the latter is rare and has been in turn subclassified into high-pressure leak (NT-HPL) and normal-pressure leak (NT-NPL), depending on the degree of intracranial pressure [1,2]. More than half of the cases of nontraumatic leaks are the high-pressure type and are due to associated intracranial tumors and hydrocephalus of varied etiology; the remaining cases are normal-pressure leaks secondary to congenital anomalies, focal atrophy, or osteomyelitis erosion of the basal structures. Atrophy of the olfactory bulb, focal bony defects in the lamina cribrosa (cribiform plate of the ethmoid bone) causing meningeal fistulae, and meningocerebral microherniations are rarely reported in cases of NT-NPL [2-4]. Two cases of NT-NPL are presented and relevant details emphasized and discussed.

Case Reports

The diagnostic criteria for NT-NPL were met in both patients, i.e., CSF rhinorrhea, no history of trauma, and no signs of raised intracranial pressure on clinical and radiological evaluation.

Patient 1

A 44-year-old man presented with a two-year history of intermittent watery discharge from the right nostril. For the first 16 to 18 months he was treated for nasal allergy and later sinusitis. The glucose content of the nasal discharge was then found to be 3 mmol/L. There was no history of trauma. Conservative treatment consisting of bed rest for four weeks was not successful, and the patient was referred to us. He had hypertension, diabetes mellitus, and asthmatic bronchitis, all controlled with appropriate drugs. Findings from clinical examination were essentially normal and no anosmia was noted. Results of routine laboratory tests were unremarkable.

The existence of opaque right anterior ethmoidal cells seen on plain skull x-ray films was confirmed by computed tomography (CT). CT scans showed two bony defects in the floor of the right anterior cranial fossa (Figure 1), i.e., a small circular anterolateral defect at the anterior end of the frontoethmoidal suture and a large circular posteromedial defect near the planum sphenoidale. Omnipaque-enhanced (Nycomed AS, Oslo, Norway) CT cisternography (OCTC) showed obliteration of the anterior half of the medial orbitofrontal sulcus on the right side (Figure 2) and filling of the anterolateral bony defect, but not the posteromedial defect, with contrast material (Figure 3). Omnipaque was seen in the right nasal cavity (Figure 4). The floor on the anterior cranial fossa was explored on the right side through a transcranial-intraductal approach. Two meningeal fistulae were found at the corresponding sites of bony dehiscence seen on radiological studies. The anterolateral meningeal fistula (2 to 3 mm in size) communicated with the anterior ethmoidal cells. The olfactory fossa was shallow, the olfactory bulb atrophied, and there was herniation of the brain tissue in the posteromedial meningeal fistula. The brain was disengaged from the fistulous tract and both defects

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Accepted for publication 5 February 1990.

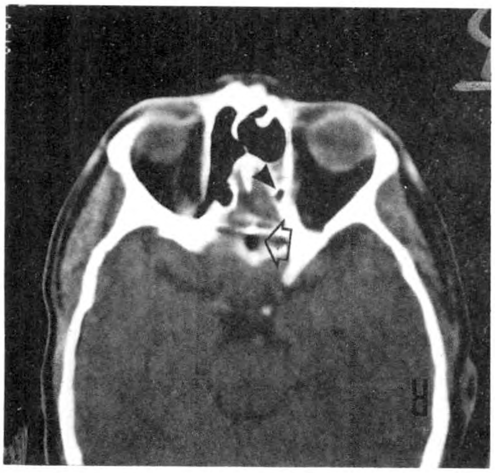

FIGURE 1. Computed tomogram showing two bony defects *(arrows)* in the floor of the anterior cranial foss on the right side.

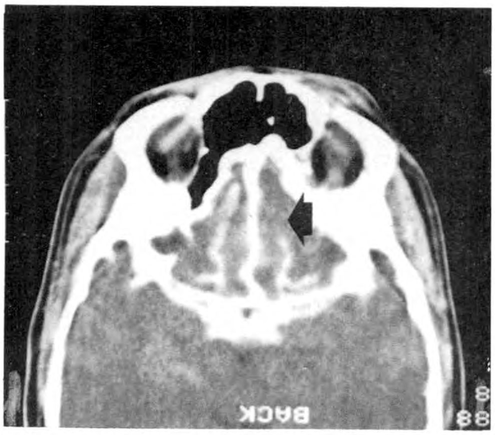

FIGURE 2. Omnipaque-enhanced CT cisternogram showing obliteration of the anterior half of the medial orbitofrontal sulcus on the right side *(arrowhead)*.

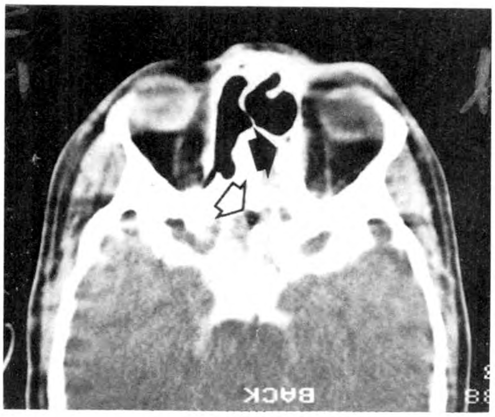

FIGURE 3. Omnipaque-enhanced CT cisternogram showing filling of contrast agent in the anterolateral defect *(arrowhead)* and nonfilling in the posteromedial defect *(open arrowhead)*.

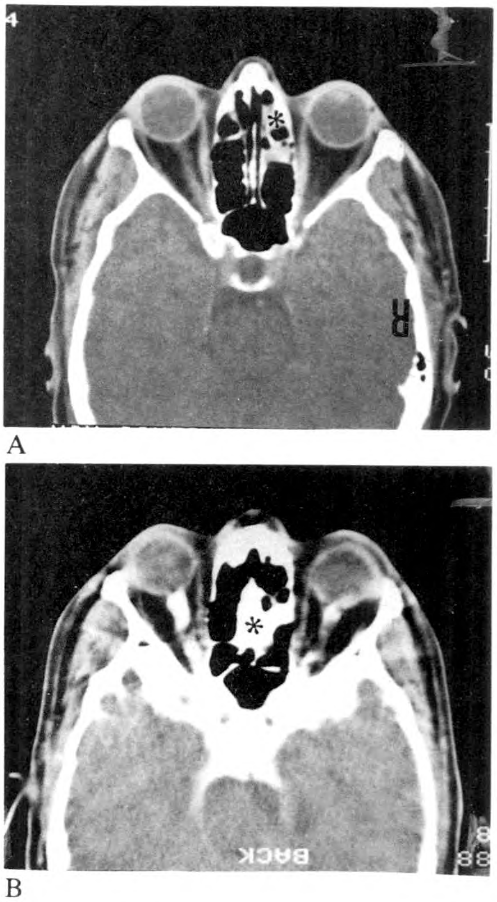

FIGURE 4. (A) Non-contrast-enhanced computed tomogram showing mucosal thickening in the right ethmoidal cells *(asterisk)*. (B) Scan with contrast enhancement showing Omnipaque in the basal subarachnoid cisterns, in the subarachnoid space around the optic nerves, and in the right ethmoidal cells and nasal cavity *(asterisk)*.

were packed with muscle. The floor of the olfactory fossa and adjacent areas were then covered with lyophilized dura mater (Lyodura; B. Braun Melsungen AG, West Germany) and fixed with a glue (Histoacryl-blau; B. Braun Melsungen AG, West Germany). No CSF rhinorrhea was noted in the immediate postoperative period or during the 9 months of follow-up.

Patient 2

A 45-year-old woman presented with a seven-year history of intermittent copious watery discharge from the left nostril. For the first six months she was treated for sinusitis, and later she was treated for allergic rhinitis for about six and a half years. There was no history of trauma. The nasal fluid was tested for glucose content, which was 3 mmol/L, and this finding prompted referral to us. She had had diabetes mellitus and hypertension for about ten years, and these ailments were controlled with appropriate drugs. Findings from clinical examination were essentially normal, and no anosmia was noted. Results of routine laboratory tests were unremarkable. Plain skull x-ray films and CT scans were normal, but OCTC showed that the left medial orbitofrontal sulcus was less delineated compared to the right. At operation, the floor of the anterior cranial fossa was explored on the left side through a transcranial-intraductal approach. The olfactory bulb was shrunken, and on lifting the olfactory bulb off the olfactory fossa, two meningeal fistulae were visualized near the root of the crista galli. An anteriorly placed meningeal fistula (2 to 3 mm in size) communicated directly with the nasal cavity. A small portion of the brain was herniating through the posteriorly placed larger meningeal fistula (4 mm in size), and the affected brain tissue was disengaged. This fistulous tract was also communicating with the nasal cavity. Both fistulae were packed with muscle and fat and were covered with lyophilized dura mater (Lyodura). No CSF rhinorrhea was noted in the immediate postoperative period or during the 10 months of follow up. The left anterior cranial fossa was explored after OCTC findings ruled out CSF leaks from the sella turcica and the petrous bone.

Discussion

Ommaya et al [1] settled the dispute over the varied terminology for the condition in which CSF leaks through the base of the skull either into the nose or into the ear without any history of trauma. Their terminology was based on the etiology of the condition: nontraumatic and traumatic [1]. The former are rare compared to the latter, and therefore misdiagnosis or failure to make a timely early diagnosis is not uncommon, as happened in both our patients. Nontraumatic leaks are more common in women over thirty years of age and are rarely associated with anosmia or intracranial aeroceles, whereas headaches are common complaints.

In cases of NT-NPL the CSF reaches the nasal cavity through the frontal sinus, the lamina cribrosa, the sphenoid roof, or the petrous bone via the middle ear cavity and the eustachian tube [5]. Nontraumatic CSF otorrhea occurs due to a bony defect in the tegmen tympani, a round window fistula, or posterior fossa defects [6,7]. NT-NPL into the nose usually occurs as the result of congenital anomalies and focal atrophy or osteomyelitic erosion of the basal structures. Nontraumatic defects, either congenital or developmental, in the anterior cranial fossa have been rarely reported [3,4]. The normal content of the olfactory fossa (olfactory bulb) or sella turcica (pituitary gland) is reduced due to focal atrophy [1,8], possibly following ischemia. The empty space thus created is filled with an arachnoidal pouch which is simply an extension of the normal CSF spaces or cisterns. This pouch enables the normal CSF pressure pulse to exert a focal continuous erosive effect analogous to excavations in the cranial vault created by arachnoidal granulations [3]. Both our patients had severe atrophy of the olfactory bulb on the side of the meningeal fistulae. O'Connell [3] described the combination of an excavated lamina cribrosa and a shrunken olfactory bulb in two patients, causing the development of a pulsating pocket of CSF over the fistula. Recently, Front and Penning [9] described three patients with recurrent meningitis but no obvious rhinorrhea in whom a pouch of arachnoid bulged through the floor of the anterior cranial fossa into the nasal cavity. Minor degrees of congenital meningeal and meningocerebral herniation can also act as an actual or potential pathway in the anterior skull base and be manifested in adult life through the occurrence of CSF rhinorrhea [2]. Small meningocerebral hernias were seen in our patients. The genesis of such a leak, aside from the role of focal atrophy, is probably related to the attainment of maximal CSF pressure in adults in association with factors such as sneezing, coughing, or other causes of normal fluctuations in CSF pressure [3]. The leaking fluid must be identified as CSF before the site of the leak can be established. Biochemical tests on the collected fluid must show glucose content of more than 1.5 mmol/L to be conclusive. The main risk of this condition is the possibility of meningitis, which can prove fatal [5].

Various methods have been used to localize the meningeal fistula. The intrathecal injection of radiological contrast materials or radioisotopes for radiographic imaging has sometimes been used. Radionuclide cisternography is a simple and reliable method that causes little discomfort to the patient [10]. Radiographic techniques commonly used include plain x-ray films that can reveal air-fluid levels in the paranasal sinuses and conventional tomograms that can show bony defects.

With CT-assisted positive-contrast (water-soluble) cisternography, the anatomical site and extent of the meningeal fistula can be demonstrated precisely by directly showing contrast material passing through the bony defect [11]. A combination of bony dehiscence and collection of contrast material within the adjacent paranasal sinuses or the nasal cavity is also useful in localization, as seen in Patient 1.

Distortion of the interhemispheric fissure, sylvian fissure, or basal sulci indicates the probability of brain herniation through the bony defect. In Patient 1, the medial orbitofrontal sulcus was obliterated in its anterior half (see Figure 2), and at operation a small meningocerebral hernia was seen in the adjacent meningeal fistula. In Patient 2, the left medial orbitofrontal sulcus was less delineated on OCTC compared with that on the right. A meningocerebral hernia was seen in the adjacent meningeal fistula. Although isotope cisternography and CT-assisted positive-contrast (water-soluble) cisternography remain the main methods for precise localization or verification of a suspected meningeal fistula, many cases of NT-NPL still remain an investigative problem [12].

The treatment for nontraumatic leaks is primarily surgical [2,13–15]. In cases of NT-HPL the cause of the high intracranial pressure, such as tumor or hydrocephalus, is treated first and repair of the fistula is undertaken only if the CSF rhinorrhea continues [16]. Obliteration of the meningocerebral herniation should accompany careful intradural repair of the fistula or fistulae, as there may be more than one defect, as seen in both our patients. Plastic repair of the floor of the anterior cranial fossa resulted in complete resolution of CSF rhinorrhea in both cases.

Acknowledgments

We thank Dr. Derek Harvey, Medical Officer In-Charge, Khoula Hospital, Muscat (Oman), for allowing us to use the hospital records, and Mrs. T. Benedicta Fernandes, Mrs. Anita Rastogi, and Mr. G. Geevarghese for their secretarial assistance in the preparation of this manuscript.

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BRAIN ABSCESS FOLLOWING ENDOSCOPIC SCLEROTHERAPY

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It is well known that transient bacteremia may occur following endoscopic sclerotherapy [1], but there are occasional reports of major complications. One hundred forty sclerotherapy procedures were done in our unit of King Khalid University Hospital, Riyadh, between August 1983 and July 1988. Of these, very few patients suffered serious complications. We report the case of one in whom a cerebral abscess developed.

Case Report

A 30-year-old Yemeni male was diagnosed as having portal hypertension due to liver cirrhosis with esophageal varices. Because of an episode of hematemesis, upper gastrointestinal endoscopy was done which revealed active bleeding from the esophageal varices. Sclerotherapy was therefore commenced, and he underwent three sessions of injection sclerotherapy of the varices without any immediate complications.

Three weeks after the third session of sclerotherapy he experienced fever, headache, lightheadedness, and two episodes of transient loss of consciousness. He was therefore admitted for further evaluation. On admission, his temperature was 38.5°C. He was conscious and oriented, but anxious. He exhibited photophobia, but central nervous system findings were entirely normal. Skin, mouth, teeth, and pharynx were normal, and there was no peripheral lymphadenopathy. He was not jaundiced but his liver span was 8 cm in the midclavicular line. There was no ascites. His spleen was enlarged 3 cm beyond the costal margin.

His full blood count showed a white cell count of 3.3×10^9/L; hemoglobin, 150 gm/L with normal indices; and platelet count of 137×10^9/L. Blood cultures were sterile and serological testing for brucellosis was negative. Liver function tests were normal except for a low albumen level of 31 gm/L (normal, 35 gm/L) and his prothrombin time was normal. An ultrasound examination of the abdomen revealed a small liver with an irregular surface and periportal fibrosis as well as splenic enlargement with dilatation of the portal vein.

On the fourth day after admission, the patient complained of severe occipital headache and photophobia, and he became restless. On examination, he was found to be disoriented and confused. His neck was rigid and Kernig's sign was elicited. Pupils were equal and reactive to light. Both fundi showed early papilledema. There was weakness of the right sixth cranial nerve, and the left plantar response was extensor.

Repeat complete blood count showed a total leukocyte count of 26.8 10^9/L; hemoglobin, 16 gm/dl; and platelets, 217×10^9/L. Differential count revealed 95% polymorphs, 3% lymphocytes, and 2% monocytes. Lumbar puncture showed turbid cerebrospinal fluid (CSF) at a pressure of 102 cm H_2O. The total white cell count was 15.6 x 10^9/L with 98% polymorphonuclear leukocytes and 2% lymphocytes. The CSF protein was 7.6 gm/L and the glucose was 0.1 mmol/L. Grams' staining of the centrifuged deposit showed gram-positive cocci. X-ray studies of the chest, paranasal sinuses, and mastoid process were normal. Computed tomographic (CT) scan of the brain showed multiple areas of cerebritis in the right parietal region. After the administration of intravenous water-soluble contrast medium, a small area of ring enhancement with cerebral liquefaction was noted (Figure 1).

Subsequently *Streptococcus milleri* was cul-

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Accepted for Publication 5 February 1990.

tured from the CSF. Treatment was commenced with parenteral benzyl penicillin, chloramphenicol, metronidazole, and dexamethasone.

On the 10th day, the patient became afebrile, his mental clouding abated, and his headache resolved. No further abnormal neurological signs were elicited. Repeat CT scan of the brain at six weeks showed resolution of the abscess (Figure 2). The patient was discharged after seven weeks of antibiotic treatment. He was followed in the outpatient clinic and showed no detectable residual neurological deficit.

Discussion

Brain abscess is a life-threatening condition and may be caused by direct spread of infection from the middle ear, paranasal sinuses, or trauma to the face and skull and hematogenous spread caused by suppuration in other organs or tissues.

Endoscopic sclerotherapy is effective in arresting bleeding from esophageal varices [2]. Its complications include transient fever, retrosternal pain, esophageal ulceration, stricture, mediastinitis, and pleural effusion [3]. In our patient, no source of infection was found in the paranasal sinuses, middle ear, lungs, or heart. Fever following endoscopic sclerotherapy usually lasts for 36 hours and may possibly be due to pyrogens in the sclerosants [4]. Our patient had low-grade fever three weeks after the sclerotherapy and this, together with disturbed cerebral function and neck rigidity, alerted us to the possibility of cerebral abscess. The diagnosis was confirmed by CSF examination followed by CT scanning of the brain.

The reported incidence of bacteremia immediately following sclerotherapy is about 5% [4,5]. It is likely that the solitary brain abscess in our patient was due to *Streptococcus milleri* infection and arose three weeks after the third session of sclerotherapy. *Streptococcus milleri* is a common inhabitant of the mouth [6]; the bacteria gain access to the bloodstream during manipulation of the endoscope in the esophagus and later settle in the brain. One study showed that *Streptococcus milleri* is the predominant organism in brain abscess [7]. Although minor complications are common following sclerotherapy, brain abscess is rare. To our knowledge there is only one previous report of a solitary cerebral abscess and this

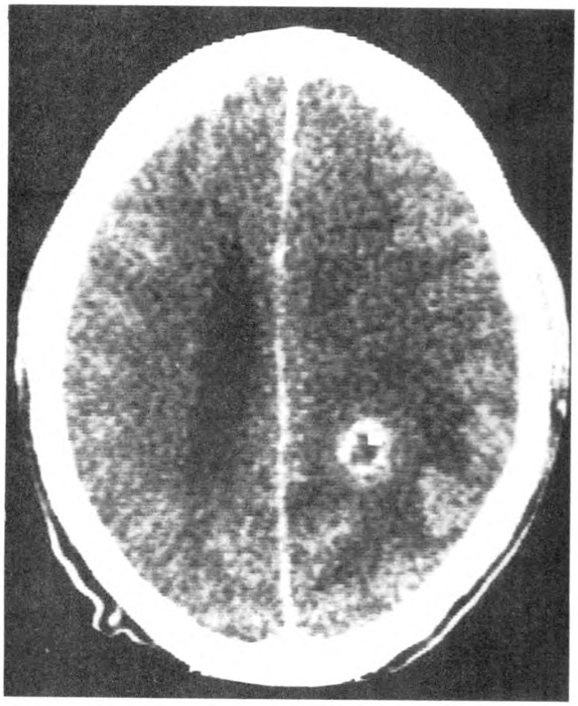

FIGURE 1. Computed tomographic scan of the brain with contrast media, showing a small area of ring enhancement with cerebral liquefaction.

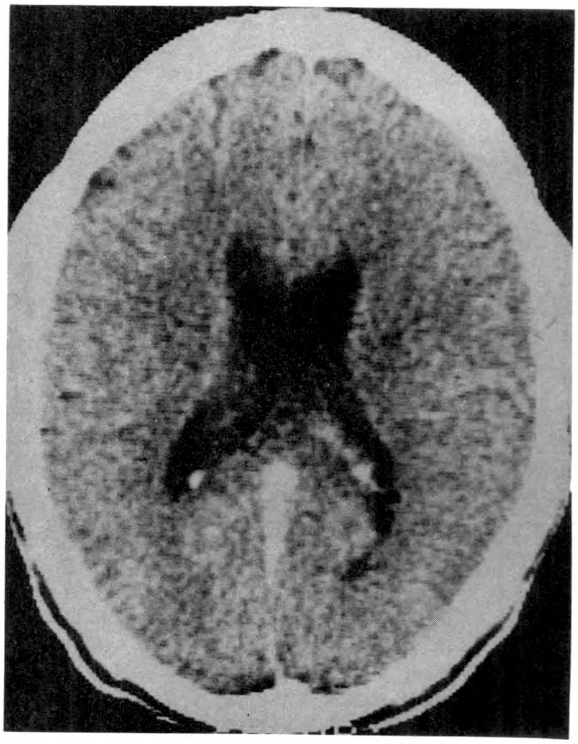

FIGURE 2. Computed tomographic scan of the brain with contrast media, showing resolution of the cerebral abscess.

suggests that, if it goes undiagnosed, it is invariably fatal [3]. Despite advances in neurosurgery and antibiotic therapy, the mortality remains as high as 40% [9]. Early diagnosis using CT and subsequent antibiotic therapy have reduced the mortality to 0 to 24% [8]. When appropriate and in the presence of suspicious symptoms, CSF examination and CT scanning should be performed in the postsclerotherapy period [8]. This will foster early diagnosis and treatment of this uncommon but fatal complication.

Acknowledgment

We thank Ms. Bennie Campos and Mr. Raj for their secretarial assistance, the endoscopy unit nurses for their assistance, and the medical photography department for their cooperation.

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ENDOBRONCHIAL HODGKIN'S LYMPHOMA

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Intrathoracic involvement of the lymph nodes, lung parenchyma, and tracheobronchial tree in Hodgkin's disease (HD) occurs in up to 40% of the cases [1–5]. Nodal and parenchymal involvement are more common and endobronchial involvement as a primary presentation is uncommon [1–4,6,7]. The lesions can be either plaque-like infiltrates with superficial mucosal ulceration or nodular masses that partially or totally occlude the lumen. Multiple lesions are usual and single polypoidal or adenomatous masses are rare [1,3]. We present two cases that presented initially as endobronchial HD and briefly review the literature.

Case Reports

Patient 1

A 22-year old woman, a nonsmoker, presented with a 6-week history of cough and labored breathing when lying down. Physical examination showed right supraclavicular lymphadenopathy, mild hepatosplenomegaly, uniformly diminished breath sounds over the left chest, and fine crepitations and wheezing over the right lower chest. Her hematological and biochemical parameters were normal. X-ray studies and computed tomographic (CT) scans of the chest showed mediastinal lymphadenopathy (Figure 1). Whole-body gallium scan showed increased activity in the anterior mediastinum and cervical regions. Lung function tests showed obstructive ventilatory impairment. Sputum showed no malignant cells or acid-fast bacilli. Bronchoscopy revealed multiple nodular masses in the carina that occluded the left main bronchus totally and the right main bronchus partially. Biopsies were not taken to avoid the risk of bleeding and further compromise of the lumen. Right supraclavicular node biopsy revealed a nodular sclerosing type of HD. Examination of needle biopsy specimens from the liver revealed unremarkable findings. A bone marrow biopsy specimen showed only reactive hyperplasia.

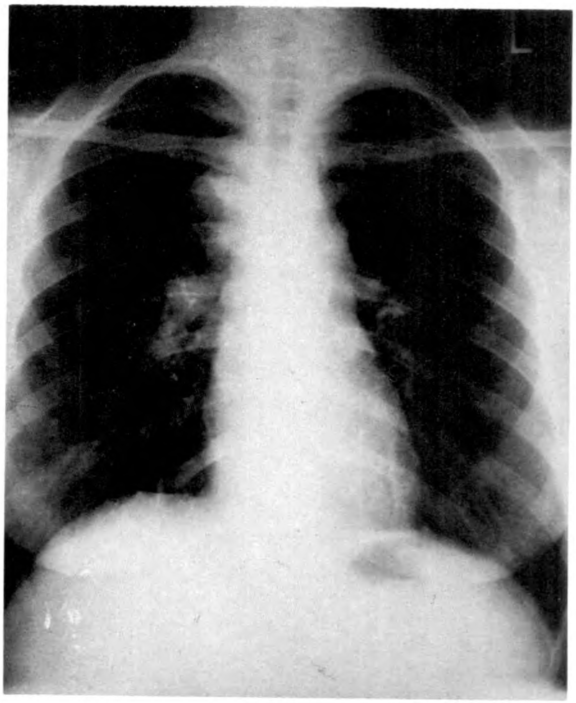

FIGURE 1. Radiograph of the chest, showing mediastinal lymphadenopathy before treatment.

Alternating mechlorethamine, vincristine, procarbazine, prednisone–adriamycin, bleomycin,

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Accepted for publication 10 April 1990.

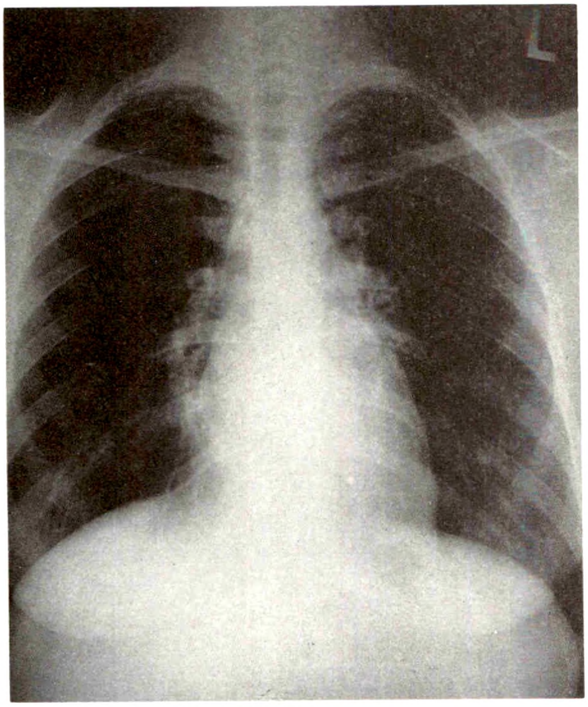

FIGURE 2. Radiograph of the chest, showing resolution of mediastinal lymphadenopathy after treatment.

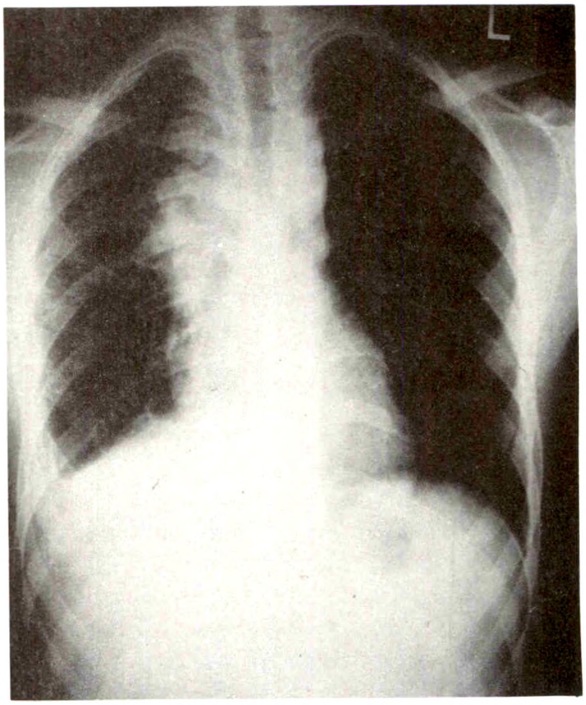

FIGURE 3. Radiograph of the chest, showing atelectasis of the right upper lobe and mediastinal lymphadenopathy before treatment.

vinblastine, dacarbazine (ABVD) chemotherapy [8] was started after determining that she had Stage $III_{ES}A$ HD. Mantle-field and upper abdominal radiation therapy was given after three cycles of chemotherapy. Repeat x-ray studies of the chest showed resolution of the mediastinal lymphadenopathy (Figure 2). Bronchoscopy done one month after the start of chemotherapy showed complete resolution of the endobronchial mass with slight concentric narrowing of the left main bronchus. She continues in complete remission, a year after diagnosis.

Patient 2

A 24-year-old man, a nonsmoker, presented with a 2-month history of dyspnea and low grade fever. Clinical examination showed no abnormality. Investigations showed a neutrophilic leukocytosis of 19.8 × 10^9/L and erythrocyte sedimentation rate of 65 mm in the first hour. Lung function tests were normal.

X-ray studies and CT scan of the chest showed mediastinal lymphadenopathy and atelectasis of the right upper lobe (Figure 3). Whole-body gallium scanning showed increased activity in the right hilar region and mediastinum and in the left paraaortic region. CT scan of the abdomen showed paraaortic lymphadenopathy.

Bronchoscopy revealed a sessile mass that occluded nearly half of the right main bronchus. Mediastinotomy was performed and a few lymph nodes were excised. Histopathological examination showed a nodular sclerosing type of HD. Examination of bone marrow revealed reactive hyperplasia. His HD was staged as III_EB and chemotherapy was instituted with an ABVD regimen [9]. Bronchoscopy done eight weeks later showed resolution of the endobronchial disease. Follow-up chest x-ray studies showed resolution of the mediastinal lymphadenopathy and expansion of the right upper lobe 3 months after the start of the treatment (Figure 4). The patient was lost to follow-up 4 months after the start treatment.

Discussion

Bronchial involvement in HD may be due to endobronchial growth, diffuse peribronchial infiltration, or pressure effect produced by peribronchial nodes [6]. The clinical features include hemoptysis, persistent chest infection, atelectasis,

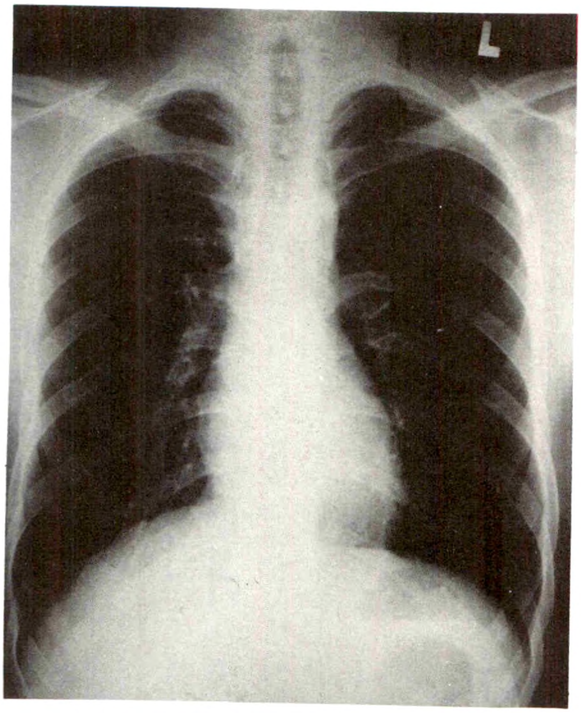

FIGURE 4. Radiograph of the chest, showing expansion of right upper lobe and resolution of mediastinal lymphadenopathy three months after the start of treatment.

paroxysmal cough, or bronchospasm. None of these are specific for bronchial lymphomas and only indicate bronchial obstruction. Only bronchoscopy can yield an accurate diagnosis.

The pathogenesis of endobronchial lymphomas remains unclear. The disease may arise from mucosal lymphoid tissue, or spread contagiously from hilar lymph nodes or through hematogenous spread [4–6,10–13]. If there is associated proximate hilar adenopathy and clear uninvolved bronchial mucosa over the endobronchial lymphoma, the cause of endobronchial lesions is likely to be due to transmural spread [10]. This appears to have been the case in both our patients. Whether endobronchial involvement signifies advanced disease is not clear. It is also not established whether there is any particular histological pattern associated with endobronchial HD [4]. In a review of 30 cases, no clear histological pattern was found [1,2,4,7,10,14]. Both our cases were of the nodular sclerosing type. It is possible that endobronchial lesions are missed in patients with HD if bronchoscopy is not done. Gallagher et al [10] found only three of their eight patients with HD had endobronchial lesions. Gribetz et al [15] found no endobronchial lesions in their 29 patients with HD. Bronchoscopy is the most accurate method for diagnosing endobronchial HD and may have an advantage over other tests in evaluating the efficacy of treatment [16]. In patients with HD, whose symptoms include those of bronchial obstruction, one should consider early bronchoscopy to evaluate endobronchial involvement.

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HIDDEN FOREIGN BODY AS A CAUSE OF RECURRENT HEMOPTYSIS

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Hemoptysis is a potentially serious condition that requires thorough investigation. The amount of bleeding is no index to the underlying pathology [1], and important causes include pulmonary tuberculosis, bronchiectasis, and chronic cardiorespiratory problems [2,3]. An inhaled foreign body as a cause of recurrent hemoptysis has received little attention in the English medical literature. Recently, Pattison et al [4] reported a case in a teenage girl. We present a case in a 67-year-old man and discuss aspects of management.

Case Report

A 67-year-old farmer was seen because of recurrent hemoptysis of 8 months' duration, associated with chest pain and dyspnea of recent onset (5 days). He had no fever or night sweats. He was a heavy smoker and a diabetic, controlled on glyburide. He had coarse crepitations over the right lower zone, where chest x-ray study showed a consolidation that was confirmed by computed tomography (CT). Repeated cytological examination of sputum and bronchial lavage findings suggested an inflammatory process but were negative for malignant cells, except for some atypical cells that suggested malignancy. Fiberoptic bronchoscopy revealed a polypoid structure in the medial basal segment of the right lower lobe which was difficult to biopsy adequately. Multiple semiblind biopsy specimens showed chronic inflammatory changes. PPD test was positive but sputum examinations were negative for acid-fast bacilli.

In view of the suspicion of malignancy because of cytological findings, a right lower lobectomy was performed. Dissection of the specimen revealed a foreign body with a leaf-like appearance embedded in a basal bronchus (Figure 1), with surrounding inflammation. Histopathological examination showed squamous metaplasia and dysplasia of the epithelium, with severe chronic inflammation and scarring in the surrounding lung tissue. The plant nature of the foreign body was confirmed by histological analysis and later identified as the skin of a pepper fruit by the Institute of Agriculture. The patient made an uneventful recovery and has had no further hemoptysis over 2 years of follow-up.

Discussion

Foreign body inhalation is more common in children and may thus be suspected as a cause of hemoptysis in that age group. In adults, however, it is less common and easily ignored, once the acute manifestations have subsided. The resultant hemoptysis may thus suggest a more sinister condition, making thorough investigation mandatory. Johnston et al [1] have stressed the importance of bronchoscopy as part of the initial investigation in men over the age of 40 who present with hemoptysis, in view of the increased likelihood of carcinoma. Our patient fell into this category.

The difficulty of obtaining an adequate biopsy from the mass, together with the suspicion of malignancy based on cytological evidence, made thoracotomy mandatory. Lobectomy was indicated by the localization of the consolidation to the right lower lobe. The presence of a foreign body accounts for the dysplasia which was thought to be malignancy because of some atypical cells seen on cytological examination. If a foreign body remains in place, this usually leads to recurrent infections,

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Accepted for publication 17 April 1990.

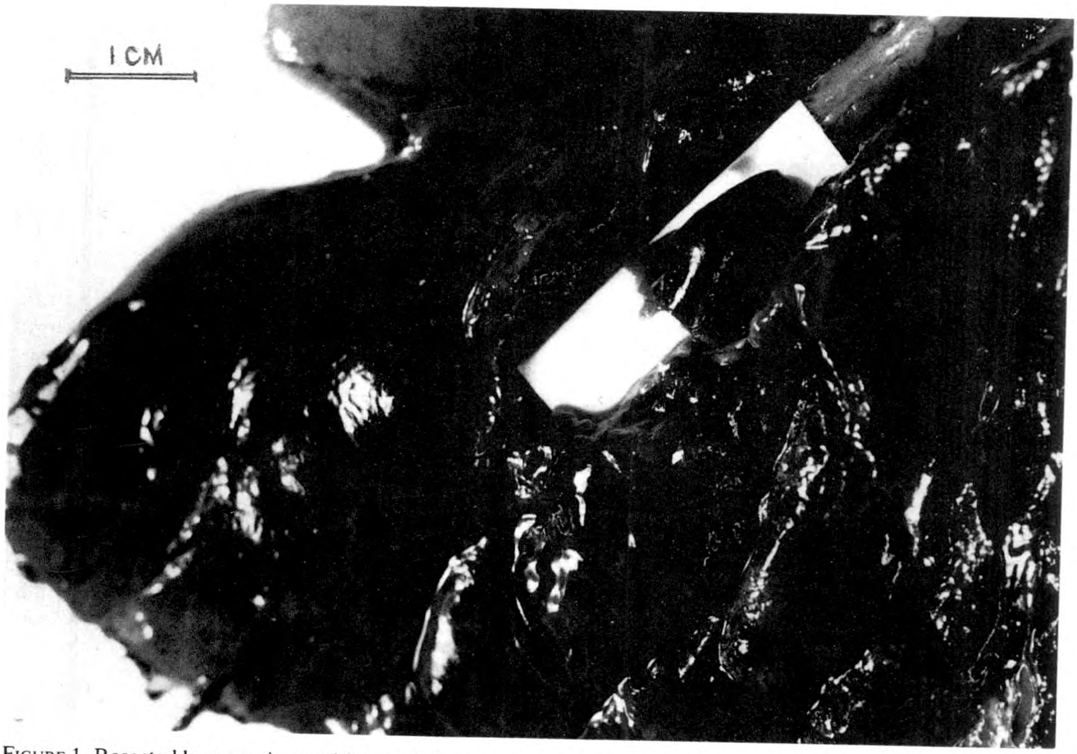

FIGURE 1. Resected lung specimen with bronchus opened to show foreign body against white background.

thus making antibiotic treatment alone inadequate. In our case, resection proved curative.

The usefulness of CT and digital subtraction angiography in localizing a foreign body has been proposed [4], especially where a chest radiograph is normal and bronchoscopy findings unhelpful. Digital subtraction angiography could have aided in the detection of the foreign body in our patient, but even with this our management would have been the same for the reasons outlined. If the foreign body is free and can be removed, resection would be unnecessary. For this reason, preoperative localization and bronchoscopic removal of a bronchial foreign body should be attempted in all cases of recurrent hemoptysis due to foreign body.

In the case reported by Pattison et al [4], the foreign body was shaped like wild barley. In long-standing cases, secondary changes may alter the foreign body so much that it is unidentifiable. Proliferation of connective tissue or epithelium around the foreign body may further increase the difficulty in identification. In our case, the foreign body was conclusively identified as the skin of the pepper fruit.

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DELAYED TRAUMATIC INTRACEREBRAL HEMATOMA: CASE REPORT AND REVIEW OF LITERATURE

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Delayed traumatic intracerebral hematoma is an uncommon serious complication of severe head injury that is associated with a high mortality. By definition, it arises in an area of the brain where intracerebral hematoma had been noted on a computed tomographic (CT) scan performed in the early postinjury period. The lesion was originally described a century ago by Bollinger [1]; however, Morin and Pitis [2] found only 24 cases reported in the literature before 1970. Baratham and Dennyson [3] in 1972 reported 21 cases out of 7886 cases of head injury seen during a ten-year period. It was only after the advent of CT that it was possible to confirm the de novo occurrence of hemorrhage in areas of the brain shown to be normal on an initial scan [4–7]. Currently, the reported incidence represents between 1.5 and 7% of the cases of severe head injury [8,9]. However, French and Dublin [10] could find only one case among their 1000 consecutive cases of head injury.

Because delayed traumatic intracerebral hematoma frequently occurs in patients with cerebral contusion, a deteriorating neurological state in such patients may erroneously be attributed to edema around a preexisting cerebral contusion causing an increase in mass effect [6]. Thus, correct diagnosis and treatment are not infrequently delayed, with irreversible neurological damage as the outcome. The value of repeated CT scanning as part of the clinical management of severe head injury patients cannot be overemphasized.

In our prospective study of 120 patients with a severe head injury (with a Glasgow Coma Scale [GCS] of 8 or below) who were seen over a one-year period, we found only one had a solitary delayed traumatic intracerebral hematoma, and this case forms the basis of our report, along with a brief review of the literature.

Case Report

A 35-year-old Omani male was admitted with a GCS of 6 (i.e., no eye opening to pain, flexion withdrawal to pain, no verbal response to pain) following a road traffic accident. He had stable vital parameters (pulse, 90 bpm; blood pressure, 130/90 mm Hg; respiration, normal) and no focal neurological deficits. There were no injuries to the chest, abdomen, or limbs. Plain x-ray studies of the skull showed no fracture and CT scan done 16 hours after the accident showed no abnormality (Figure 1). With symptomatic management, his level of consciousness improved to a GCS of 11 (i.e., spontaneous eye opening, localizing to pain, voicing noise on pain). On the fourth postinjury day, a rapid-onset left hemiplegia developed and he became restless. However, his vital signs remained stable and an urgent CT scan (Figure 2) was performed that revealed a moderate-sized right posterior frontal intracerebral hematoma with surrounding edema, producing slight mass effect. He was treated conservatively, and this consisted of mannitol and dexamethasone therapy along with nursing care and physiotherapy. Over three weeks, his level of consciousness improved to a GCS of 15, and the left hemiplegia abated to a power grade of 4–5/5. Repeat CT scan at three weeks (Figure 3) showed considerable resolution of the right posterior frontal intracerebral hematoma and no mass effect. He was continued

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Accepted for publication on 12 May 1990.

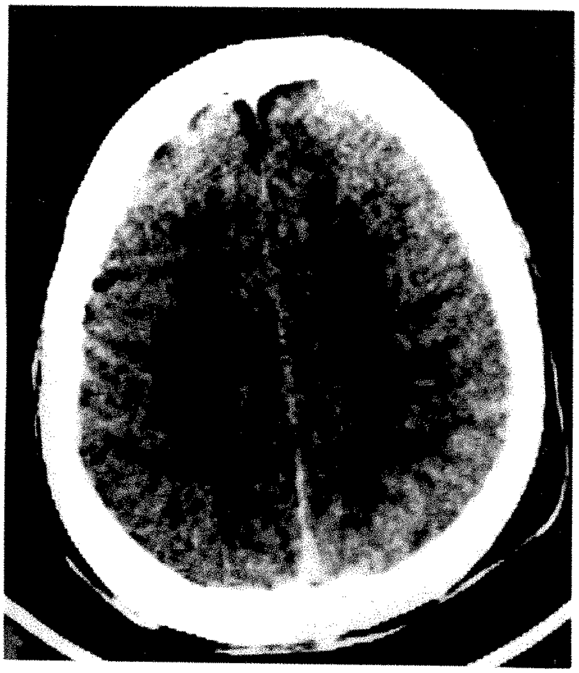

FIGURE 1. CT scan 16 hours after the accident, showing no abnormality.

on physiotherapy for six weeks, with good improvement.

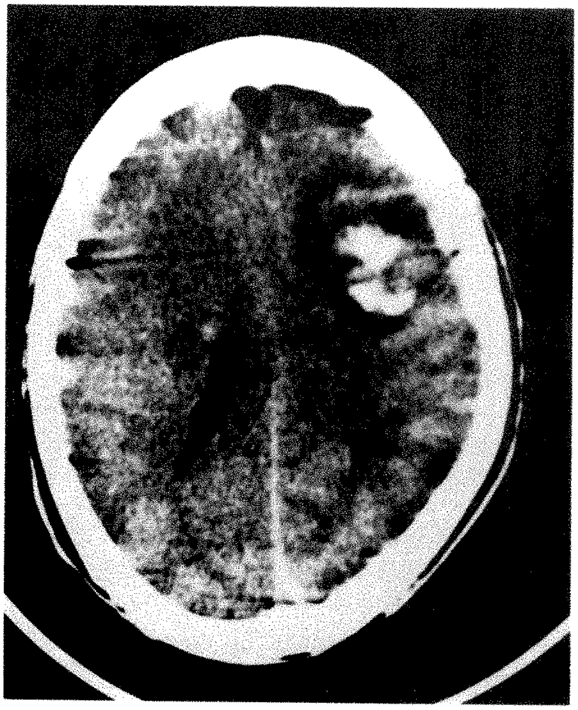

FIGURE 2. CT scan on fourth postinjury day, showing a right posterior frontal intracerebral hematoma with little mass effect.

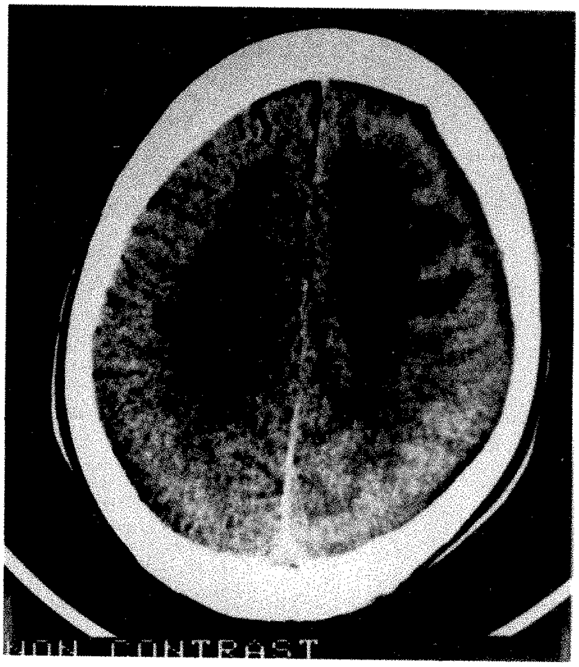

FIGURE 3. CT scan three weeks following the accident, showing resolving right posterior frontal intracerebral hematoma.

Discussion

Of the various types of traumatic intracranial hematoma, the appearance of the intracerebral type is most likely to be delayed–the so-called delayed traumatic apoplexy of Bollinger [11]. Delayed traumatic intracerebral hematoma is a serious complication with a high mortality of from 30 to 72% reported for various series [2,3,12–15]. Delayed diagnosis and treatment is a common cause of this high mortality [3], although the severity of the initial impact and secondary insults are also contributory [15].

The etiology of delayed traumatic intracerebral hematoma has been the subject of considerable speculation. Focal brain injury is thought to result in decreased vascular resistance, allowing an increased head of arterial pressure and increased blood flow to be transmitted to an already traumatized capillary–vascular bed, with resultant hemorrhage into the cerebral parenchyma [2,7,13,16]. Compression of the brain caused by a hematoma or edema can produce ischemia, necrosis, and secondary hemorrhage [12]. Mechanical distortion producing ischemia and infarction may cause delayed traumatic intracerebral hematoma [17]. Severe head trauma can also result in coagulopathies which in turn cause cerebral hemorrhage [18,19]. Recent data indicate that delayed traumatic intracerebral hematomas frequently occur in patients with disseminated intravascular clotting and fibrinolysis [18,19]. Baratham and Dennyson [3] attempted to correlate the development of delayed intracerebral hemorrhage with hypoxic or hypercarbic episodes. The local loss of autoregulation from focal trauma coupled with increased blood flow from hypoxia and hypercarbia or stagnation from elevated venous pressure could enhance diapedesis, and therefore the gradual development of a hematoma.

Baratham and Dennyson [3] stated that delayed traumatic intracerebral hematomas tend to arise in elderly patients in the seventh or eighth decades of life, with a deterioration in consciousness after a lucid interval lasting hours to days. However, our patient was a young Omani male (35 years old) who was unconscious on admission with a GCS of 6, when delayed traumatic intracerebral hematoma developed on the fourth postinjury day. His state of consciousness had already improved to a GCS of 11, when there was rapid onset of left hemiplegia. Delayed traumatic intracerebral hematoma may develop within 24 hours of injury [4,10]. The clinical signs are frequently insidious. In an clinical setting, a deteriorating state of consciousness, a newly developed third nerve palsy, or a rise in intracranial pressure may be secondary to delayed traumatic intracerebral hematoma, progressive edema around a cerebral contusion, or a cerebrovascular episode [6,18]. The real advantage of the CT scan lies with its ability to show that portions of a parenchymatous lesion are hematoma, contusion, and edema. Gentleman et al [14] contended that a patient whose admission CT scan is normal will not sustain delayed traumatic intracerebral hematoma. However, the first CT scan seen in our patient was entirely normal, signifying its rarity and underlining the fact that a normal CT scan at admission does not rule out the possible delayed development of an intracerebral hematoma. A delayed traumatic intracerebral hematoma should be suspected in any patient with severe head injury who shows clinical signs of deterioration with or without a lucid interval.

Surgical treatment is required for cases of delayed traumatic hematomas, but depends on the amount of mass effect, the location of the mass, and whether there is a discrete hematoma. Clinical and not radiological indications must predominate in the decision to perform surgical intervention [10,20]. Many lesions can be monitored by repeat CT scans without an operation. However, prompt craniotomy, when necessary, for removal of a large delayed traumatic intracerebral hematoma can yield gratifying results [21]. Our patient was treated conservatively and responded well to this approach.

Repeat CT scans in patients with severe head injuries help monitor the possible formation of a delayed traumatic intracerebral hematoma, and allow for proper management before irreversible brain damage occurs.

Normal initial CT scans in the immediate post-injury period do not rule out the possible later development of an intracerebral hematoma. A high index of suspicion must be maintained to allow for its early recognition and management.

Acknowledgment

We thank members of the Department of Surgery and Medicine, Armed Forces Hospital, Muscat, who referred this case and Mrs. Anita Rastogi for excellent secretarial assistance in the preparation of this manuscript.

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Letters to the Editor

The *Annals of Saudi Medicine* welcomes letters to the Editor from its readers. They may be on any topic, though the Editor especially encourages discussion of papers published in the *Annals*. Letters should be no more than 100 typewritten lines in length, typed double-spaced, and submitted in triplicate. Letters may include one figure or brief table and up to five references. Submission of a letter constitutes permission for the *Annals* to use it for publication. Letters should not duplicate similar material being submitted or published elsewhere, and the *Annals* reserves the right to edit letters submitted. Letters referring to a recent *Annals* article should be received within 6 weeks of the article's publication.

Traumatic Malocclusion of the Mandible: The Essence of Balanced Occlusion

To the Editor: In the science of dentistry, balanced occlusion is paramount in achieving a harmonious and functional relationship of the natural dentition. Occlusal forces distributed bilaterally over a maximum number of teeth result in minimal muscle tension and stability of the condyles in the glenoid fossae. If this stability is altered in any way through trauma or pathology, the occlusal load will be destructive to the remaining dentition, and worse, the condyles could become fulcral centers of damage to the periodontal health of the posterior teeth.

This report describes a prosthodontic rehabilitation done to re-establish maximum occlusion following traumatic injury to the mandible.

A 47-year-old Saudi man was involved in a motor vehicle accident in 1984, at which time he suffered a compound comminuted fracture of the body of the right mandible and fractures of the right and left condyles. The patient was initially treated in the operating room by the otolaryngologist with open reduction and fixation of the mandibular body and condyles. After the arch bars were applied, the patient was placed in intermaxillary fixation. Three weeks later, the intermaxillary fixation was released and deviation of the mandible to the right of midline with complete non-contact of the anterior teeth was found (Figure 1). The patient experienced moderate pain in the right condylar area upon closure and complained of inability to masticate his food properly. He was thus referred to the staff oral surgeon, who recommended a bilateral split sagittal osteotomy to correct this "open bite." The patient refused the oral surgical procedure and chose the more conservative measure of installing a removable partial denture overlay to achieve maximum occlusion.

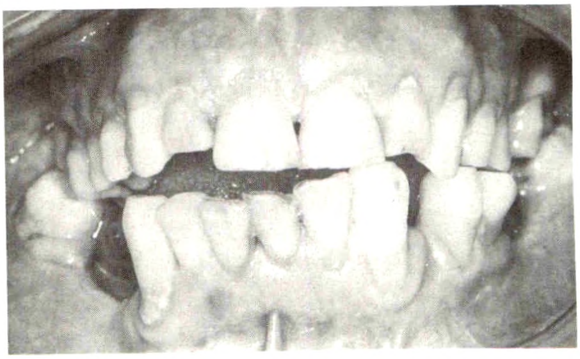

FIGURE 1. Patient's acquired centric occlusion. The only centric stop on the right side are second molars.

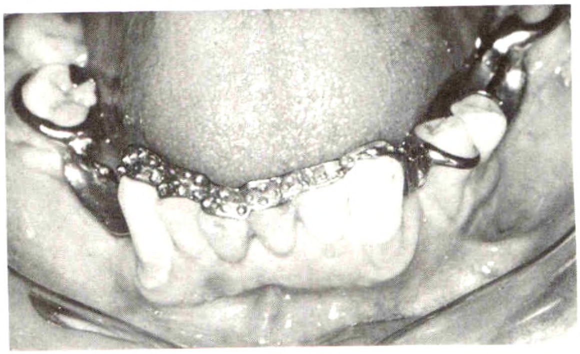

FIGURE 2. Metal framework in place. The framework was cast in Type-IV gold, as malleability, tooth contour adaptation, and thinness of the metal were important in achieving comfort for the patient.

Because the injury had caused extreme malposition of many teeth, Type-IV gold was used in the framework casting to take advantage of its malleable property which would allow for maximum seating (Figure 2). Because the patient became accustomed to the centric occlusion, no further attempt was made to disturb the maxillomandibular relationship.

The overlay veneers were finished in photo-cured microfill composites (Dentacolor; Kulzer and Co. Friedrichsdorf, FRG), which are superior to unfilled resin with regard to compression strength, surface hardness, and abrasion resistance [1] (Figure 3).

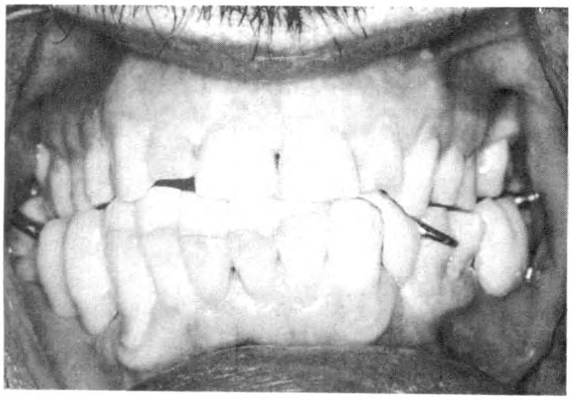

FIGURE 3. Completed partial overlay. The overlay veneers are photocured microfill composites.

Schuyler [1] considered dentition to be perfectly balanced in centric and in all eccentric positions when a muscular force is evenly applied bilaterally. Any occlusal load will then be borne by all teeth from the central incisors to the last molars. Prosthodontic rehabilitation should be directed toward aligning these forces with the long axes of the teeth.

One of the most destructive forms of malocclusion is premature (deflective) contacts borne by only a few posterior teeth [2]. Ideally the jaw functions as a Class III lever system. Any deviation in this "kinesthetic relationship" among muscles, ligaments, and teeth changes the lever system from a Class III to a Class I lever system, resulting in an efficient but devastating force imposed on teeth and the periodontium. The re-establishment of an ideal occlusion must then be accomplished through prosthodontic rehabilitation.

Schuyler [3] listed the most important functional objectives of occlusal rehabilitation as : (1) a static centric occlusion in harmony with the centric maxillomandibular relationship; (2) an even distribution of stress in centric occlusion over the maximum number of teeth; and (3) masticating efficiency that involves uniform contact and an even distribution of stress on eccentric tooth inclines.

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The Use of Sodium Valproate in Resistant Rheumatic Chorea

To the Editor: We report a case of a patient who had long-standing Sydenham's (rheumatic) chorea and whose involuntary movements were effectively controlled by sodium valproate. Other medications had been ineffective. This further substantiates our previous report [1], in which we demonstrated the efficacy of sodium valproate as the initial therapy in a group of children with rheumatic chorea of recent onset.

A 7-year-old girl presented with a two-year history of generalized chorea which was severe enough to interfere with her attending school.

Physical examination revealed severe generalized choreiform movements. Heart findings were normal and all joints had normal range of movement. The following investigations were normal: antistreptolysin O titre, erythrocyte sedimentation rate, serum copper and ceruloplasmin, C reactive protein, anti-DNA antibodies, circulating immune complexes, thyroid function tests, electrocardiography, and chest x-ray studies.

She had received several medications during the two years prior to presentation, but without benefit. These included haloperidol, chlorpromazine, phenobarbital, and diazepam. Valproic acid treatment was initiated at a dosage of 20 mg/kg/day (300 mg twice daily), with no other medications. The choreiform movements gradually diminished over seven days and had disappeared completely by 14 days. There were no side effects and no recurrence of abnormal movements after discontinuation of valproate and during one year of follow-up.

Recently, there have been a growing number of reports on the use of sodium valproate in movement disorders, including rheumatic chorea [1,2].

The precise mechanism by which valproate controls the involuntary movements in Sydenham's chorea is unknown. However, valproate is known to raise levels of gamma aminobutyric acid (GABA), an inhibitory neurotransmitter. Thus, the increased GABA concentration may exert its effect through modification of GABA-ergic synaptic transmission, thereby controlling the abnormal movements [3,4].

Based on the findings from the present report and those of others, sodium valproate appears to be a successful initial therapy for patients with rheumatic chorea of either recent onset or prolonged duration.

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Breastfeeding Practices in Tathleeth Area

To the Editor: Although the topic of breastfeeding has been dealt with in many papers originating from urban areas of Saudi Arabia [1–4], there has been little written with respect to the rural areas of the Kingdom. Therefore we undertook to examine the pattern in Tathleeth, a small rural town situated in the desert about 240 km from Abha, which is the administrative headquarters of the Asir Province. Tathleeth is an underdeveloped and relatively remote area. Most of the inhabitants are bedouins and illiteracy is common.

The subjects for the study consisted of 226 randomly selected Saudi children (males, 147; females, 79; aged, 1–24 mo) seen at the pediatrics outpatient clinic of Tathleeth General Hospital. Information was obtained by means of a questionnaire given to both parents of each child and included questions concerning the socioeconomic status and educational background of the parents, whether the child had been breastfed, and the duration, timing, and reasons for discontinuation of breastfeeding, as well as when bottlefeeding and solid foods were started.

Forty-six of the mothers were primiparous while the rest were of varying parities; 70 of the mothers had borne more than five children.

No relationship was noted between breastfeeding and parity nor with place of birth (i.e., hospital or home), which was also examined as a possible factor in breastfeeding practices. Of the 226 children, 51.7% had been breastfed only, 13.2% bottlefed only, and 35.0% had been both breast- and bottlefed. The duration of breastfeeding showed a drastic decline from 86.7% at 1 month of age to 44.2% at 6 months. Only 7% of the children were still being breastfed at 24 months.

Various reasons for discontinuation of breastfeeding were given by the 30 mothers who had stopped breastfeeding when their child was 6 months of age. For most it was because of perceived inadequate lactation, but other reasons included illness of the child or mother and new pregnancy, reasons cited in other studies of breast-feeding practices [4,5].

The finding in the present study that only 51.7% of the children were wholly breastfed contrasts with the 63% incidence reported from Dammam [3], 58.1% from Qassim [6], and the 90% previously reported from the rural Asir area [7]. However, most of the studies were conducted about ten years ago, and as a recently conducted study in Riyadh [8] confirmed, there has been a general decline in the incidence of breastfeeding, both in urban and rural areas of Saudi Arabia.

Tathleeth's relative isolation from outside influences such as television and the widespread illiteracy of the populace do not implicate outside factors as the source of these changing patterns, factors which could account for the changes seen in more urban areas. In fact, the reasons cited by the mothers in this study reflect individual circumstances. An additional observation was that not only are fewer women breastfeeding, but they are doing so for less time.

Other possible reasons for this changing pattern of breastfeeding include lack of proper motivation, easy availability of commercial formulae, high purchasing capacity, single family system with increased separation from the influence of elders, insufficient support given to mothers by health personnel, and lack of antenatal care. Improved education of the mothers to the importance of breastfeeding may help to reverse this decline in the practice of breastfeeding.

Acknowledgments

We thank Mohammed Syed Khoban, Director of Tathleeth General Hospital, for his valuable help, Professor Aderele for his critical review, and Miss Margaret and Miss Ninfa for their expert secretarial assistance.

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Breast Carcinoma in Northern Nigeria

To the Editor: Breast carcinoma continues to pose a worldwide problem with respect to both early detection and effective therapy, but the magnitude of the problem varies from one geographical setting to another [1]. Jos University Teaching Hospital, a 515-bed hospital connected with Nigerian University, has an annual admission rate of 50,310 patients, serves a population of well over 14 million people, and is one of the tertiary centres for treatment of malignant lesions in the country. Patients are referred both from the Government General Hospital and from private clinics.

From January 1979 to December 1984 there were 78 new referrals with histologically proven breast carcinoma, for an average of 13 new cases a year. The mean age at presentation was 43 years (range, 20 to 68 years). Most of the patients (88.7%) were married. Parous patients constituted 90.2%, with 73.2% having had more than three issues. All parous patients had at one time or other breastfed their infants; the average duration of suckling was 9 months, 2 days.

Family history of breast cancer was an uncommon observation and was noted in only 2.8% of the cases. The duration of history before presentation ranged from 2 months to 10 years (mean, 1 year and 3 months), showing that most patients from this part of the world present very late. In this series, 60.6% of the patients were in Manchester Stages III and IV at presentation. In the same vein, 81.4% of the patients showed axillary node involvement. This contrasts with 40% observed for white Americans and 36.59% observed for black Americans [2]. However, in a series reported from Jordan, axillary node involvement was observed in 74.6%.

Female breast cancer generally occurs earlier in the Nigerian population; age range in our study was 25 to 55 years while that reported in the Western literature was 35 to 55 years (Figure 1.) In this study the correct ages of only 64 patients could be ascertained. A recent report from South Eastern State of Nigeria cites an at risk age of 25 to 50 years [4].

Surgery still remains the mainstay of treatment in our environment. Radiotherapy is not yet readily available in all centres. Hormonal manipulation in the form of oophorectomy is used for pre-

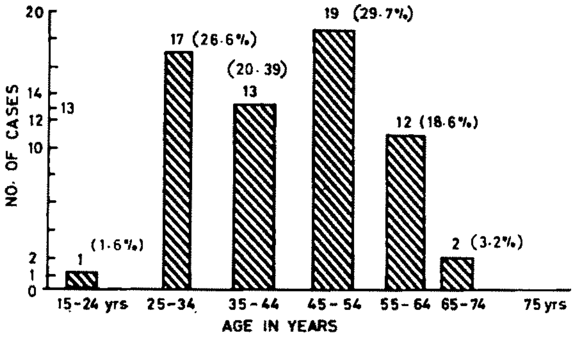

FIGURE 1. Age range of 64 patients in our study.

menopausal patients, with tamoxifen administered to patients in all age groups. Combination chemotherapy is used in advanced cases.

Our crude three-year survival figure is 20.9%, with a five-year survival of 12.5%. These rates undoubtedly reflect the advanced disease state that exists in our patients.

Because of multiparity and habitual breastfeeding, women in this geographical region are prone to ignore breast disease.

Unfortunately women in our society first seek care from traditional healers before attending hospital, by which time the disease is advanced. Eventually, all patients end up at the hospital. Given that parity, lactation, and early age at first pregnancy are a few of the generally accepted determinants and are relatively common in our population of women, it can be argued that the low incidence of breast cancer in our environment indicates our population is at low risk. Moreover, the sophistication of an animal fat–rich diet has not yet reached our society.

Within the past ten years, both the Nigerian Cancer Society and the Nigerian Medical Association have been waging a rigorous campaign aimed at increasing public awareness of this debilitating disease. Though the yearly incidence is not increasing, it is hoped that more women will present at earlier stages and that the management of breast cancer will cease to be just the palliative care of advanced mammary carcinoma.

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ACKNOWLEDGMENTS

The Editorial Board of the *Annals of Saudi Medicine* would like to thank the following individuals who have reviewed articles for Volume 10, 1990.

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Symposium Abstracts

FIFTH ANNUAL PEDIATRIC SYMPOSIUM

Sponsored by the Joint Board for Postgraduate Medical Education
Security Forces Hospital, Riyadh
7-8 Shaban 1410
(4-5 March 1990)

CHILD AND ADOLESCENT DIABETES MELLITUS, HOW BIG IS THE PROBLEM?, JW Farquhar, University of Edinburgh, Edinburgh, Scotland

In Northern Europe and America insulin-dependent diabetes mellitus (IDDM) is the second most common chronic disorder of children. It is a pernicious disease, and 70 years after the discovery of insulin, remains a principal cause of disability. The cost of treating IDDM need not be great but the long-term personal and economic burdens are enormous when complications develop. The constraints experienced by both parents and patients may and often do affect the quality of life. Present epidemiological studies establish that the incidence of the disease is rising steeply, and where good treatment exists, its prev-alence is increasing at an equally steep rate. Such observations depend on registering all diabetics and on observing their progress over many years. New technology facilitates the keeping of such information but this technology must first be made available. Cooperation between community medicine specialists and clinicians is necessary. Ultimately a concertive cooperation effort at observation among nations may reveal the cause. IDDM is known to occur in Arab children and is reported from Saudi Arabia. Will it increase as rapidly here as in the West, and if so, for what reason, and will the clinical medical services be prepared for it?

CHILD AND ADOLESCENT DIABETES MELLITUS: HOW GOOD IS THE TREATMENT?, JW Farquhar, University of Edinburgh, Edinburgh, Scotland

Judgment of success is rate-limited by the slow progress of vasculopathies over one, two, or more decades. Treatment programs carried out during 1950 to 1975 can be assessed now and during the next decade. Short-term studies attract funding and meet immediate needs, but complete long-term studies are difficult to carry out and therefore rare. Much of our treatment is difficult to reconcile with optimal child rearing. Much of our clinic and office management bears close examination through the eyes of our patients. Education, motivation, and support are interdependent and fundamental to success. They are facilitated by professional outreach into the community. As children enter adolescence, they become more resistant to direction and regimentation. Motivated young diabetics in clinics may be the "wasted resource" needed to complete the management team. Their views on clinic structure and function and on community activity should be heard.

CONGENITAL HYPOTHYROIDISM: RIYADH ARMED FORCES EXPERIENCE OVER THE LAST TEN YEARS, MA Majeed-Saidan, B Joyce, M Khan, H Hamam, Department of Pediatrics, Armed Forces Hospital, Riyadh

The total number of infants screened from April 1985 until the end of December 1989 was 39,667. Seventeen children with congenital hypothyroidism were diagnosed, 15 in the neonatal period, 12 of these on the neonatal screening program (ten cord blood and two on spot blood test at 7 days). This makes the incidence of congenital hypothyroidism in our screening program one in 13,305 live born. The period of follow-up was between 3 months and 10 years, and all patients seem to be normal both physically and intellectually. There are two families with more than one child affected, and one involving twins. Thirteen I^{131} thyroid scans were done. Eight showed a picture of dyshormonogenesis and in three there was no thyroid tissue detected. Behavioral problems were noted in two children with normal development.

CURRENT APPROACHES TO NEPHROSIS IN CHILDREN, KN Drummond, Department of Nephrology, Montreal Children's Hospital, and Department of Pediatrics, McGill University, Montreal, Quebec, Canada

Although nephrosis in childhood has many synonyms and a number of variants, it is basically one disease with a spectrum of manifestations. Its characteristics are: the nephrotic syndrome, no hypertension, hematuria or reduced glomerular filtration rate, selective proteinuria, normal serum C3 levels, absence of immune glomerular deposits, and steroid responsiveness. At least half of the patients have one or more relapses, but even with many relapses, the natural history is characterized by improvement and remission as puberty supervenes. The goal of treatment is to treat and prevent relapses while the disease runs its course and to maintain normal growth and good health without inducing untoward side effects from therapeutic or prophylactic regimens. This is possible in the great majority of cases. Each relapse brings potential complications such as sepsis and intravascular coagulation. Current approaches include a longer period of remission consolidation following relapse and the use of prophylactic regimens over a much longer period than has been previously done. Cyclophosphamide, levamizole, and cyclosporin have a role in managing relapsing nephrosis and also in some steroid-resistant cases, but prednisone therapy remains the cornerstone in treating childhood nephrosis.

DIABETIC NEPHROPATHY: A CHALLENGE FOR THE PEDIATRICIAN?, KN Drummond, Department of Nephrology, Montreal Children's Hospital, and Department of Pediatrics, McGill University, Montreal, Quebec, Canada

Diabetic nephropathy (DN) is the major life-threatening complication of insulin-dependent diabetes, affecting one third of patients with a peak incidence at 15 years after onset of diabetes. DN is the most common cause of end-stage renal disease in North America, accounting for 25% of the cases of renal failure. The clinical expression of DN (proteinuria, hypertension, falling glomerular filtration rate) is uncommon during childhood. However, it is clear that functional and pathological changes are initiated at onset of diabetes and progress silently at a subclinical level until microalbuminuria, hypertension, overt proteinuria, and a declining glomerular filtration rate appear. By the time clinical DN surfaces, glomerular lesions are already advanced, and progression to renal failure is difficult to arrest. Thus, for preventive intervention to be effective, it is crucial to identify patients at risk before irreversible damage is done and to alter the process before it has begun an inexorable course. This requires an understanding of the early pathogenesis of DN so as to isolate factors which are amenable to intervention and a means of identifying the 30% of patients at risk who are destined to develop DN. The principal pathogenesis factors appear to be glycemic control, and inherited tendency for hypertension and other undefined genetic forces, hemodynamic changes such as glomerular hyperfiltration and raised intraglomerular pressure, intrinsic properties of the kidney, and possibly dietary protein intake. The challenge to pediatricians is, as in the case of many disorders which find clinical expression in adulthood, to develop strategies which, if applied to children with diabetes, will reduce or prevent the development of DN as an adult.

CYCLOSPORINE THERAPY IN NEPHROTIC CHILDREN WITH FOCAL SEGMENTAL GLOMERULOSCLEROSIS (FSGS): EARLY EXPERIENCE AT KFSH&RC, E Al-Sabban, S Sanjad, King Faisal Specialist Hospital and Research Centre, Riyadh

Five children (four girls, one boy) aged 1½ to fourteen years with steroid and cyclophosphamide resistance with biopsy-documented focal segmental glomerulosclerosis were treated with cyclosporine A (CSA). CSA was started at 5 to 7 mg/kg/day divided BID and titrated to maintain a trough level between 100 and 300 ng/ml (whole blood radioimmunoassay). Therapy was considered failed if patients were treated for 12 weeks and showed no evidence of partial or full remission of their disease. Two patients went into full clinical remission with normalization of their serum albumin, serum cholesterol, and tri-glyceride levels. One patient showed partial response, whereby the generalized edema was easily controlled with marked reduction in her proteinuria and increase in her serum albumin level as well as decreased serum cholesterol and triglyceride levels. Two patients showed neither total nor partial response. Hirsutism was the only recognized complication in those treated patients. No evidence of nephrotoxicity was detected. None of our patients developed hypertension. Our results suggest that CSA therapy trials should be considered in steroid-resistant nephrotic children with focal segmental glomerulosclerosis, provided treated patients have normal serum creatinine levels with close monitoring of CSA serum levels to avoid major side effects.

BACTERIAL MENINGITIS: SULEIMANIA CHILDREN'S HOSPITAL EXPERIENCE, A Abanamy, M Shuja, M Cheriyan, H Salman, S Ghazal, M Khalil, Suleimania Children's Hospital, Riyadh

Bacterial meningitis continues to be the most serious infection during childhood. We present 98 cases of bacterial meningitis proven by positive culture of cerebrospinal fluid. These cases were selected from more than 200 cases admitted to our hospital from 5–1405 to 1410 with a presumptive diagnosis of bacterial meningitis. We discussed the clinical features at the time of admission, salient laboratory features, and hospital course. The most common organisms isolated from cerebrospinal fluid were *Haemophilus influenzae, Streptococcus pneumoniae,* and *Neisseria meningitidis*. A comparison of antibiotic treatment with ampicillin and chloramphenicol versus third-generation cephalosporin will be presented. The data about various complications such as convulsions, secondary fever, and hydrocephalus will be presented. We also discussed audiometric findings and developmental assessment in the follow-up of some of these patients.

TREATMENT OF DIABETIC KETOACIDOSIS IN CHILDREN: A RECENT APPROACH, A Abanamy, H Salman, M Khalil, G Basset, D Roy, Suleimania Children's Hospital, Riyadh

Diabetic ketoacidosis in children is a life-threatening emergency. It is a unique state of hyperglycemic hypertonic dehydration, with ketotic acidemia. Its treatment remains difficult because of its potential "iatrogenic" complications (hypoglycemia, hypokalemia, and, especially rare, brain edema and herniation). In recent years, most protocols of treatment used continuous intravenous insulin infusion in small doses and prudent rehydration during the first hours of therapy. We compared two groups of patients treated in our hospital with two different protocols. Protocol I, used in 23 patients, consisted of an intermittent high dose of insulin injection (subcutaneous or intramuscular) and rehydration volumes 3 to 4 L/m^2 over twenty-four hours. Protocol II, used in 15 patients, consisted of low-dose continuous intravenous insulin therapy and reduced fluid volume infusion (1.5 to 2 L/m^2) over twenty-four hours. The type of fluid and potassium supplementation were similar in the two protocols. Despite the significant reduction in the amount of insulin and fluids administered, protocol II was as effective and safe as protocol I, and furthermore, easier and more applicable in any center.

CELIAC DISEASE IN RIYADH, SAUDI ARABIA: EXPERIENCE IN KING KHALID UNIVERSITY HOSPITAL, RIYADH, AMA Abdullah, Faculty of Medicine and King Khalid Univesity Hospital, King Saud University, Riyadh

The clinicopathological features are described for 19 children with celiac disease seen at King Khalid University Hospital, Riyadh, over a five-year period. There were 12 males and seven females, with a mean age at presentation of 4.5 (range, 1.25–10.5) years. The mean age of introduction to cereals was 0.7 (range, 0.3–1.5) years, while the mean age of onset of symptoms was 2 (range, 0.3–8) years. The main presenting symptoms were diarrhea in 17 patient (89%), failure to thrive in 13 (68%), and abdominal distention in ten patients (52%). One patient presented with constipation and one patient presented with pica. The main physical signs on examination were abdominal distention in 16 patients (84%), wasting in 15 patients (78%), pallor in 12 patients (63%), edema in five patients (27%), and short stature in one patient (5%). At presentation, the mean hemoglobin level was 9.2 (range, 8.3–10.2) gm/dl. The mean folate level was 1.4 (range, 0.8–2.3) ng/ml. The mean blood D-xylose after 1 hour was 0.9 (range, 0.17–1.1) mmol/L. The initial jejunal biopsy showed subtotal villous atrophy in every patient. Repeat biopsy showed normal appearance of villi in 10 patients while on a gluten-free diet and subtotal villous atrophy after rechallenge with gluten in four patients. There was considerable delay in the diagnosis of celiac disease after the onset of symptoms.

CHILDREN WITH AMBIGUOUS GENITALIA: CAUSES, MEDICAL, SOCIOCULTURAL AND RELIGIOUS ISSUES RELATED TO MANAGEMENT IN SAUDI ARABIA, MA Abdullah, SA Al-Habib, M Katugambola, N Jurrayan, A Sammari, M Niazi, Security Forces Hospital and King Khalid University Hospital, Riyadh

Ambiguous genitalia in a newborn is a medical emergency requiring expert judgment, specialized laboratory tests, and skilled surgery for optimal long-term results affecting both patients and family. Children who have had the wrong sex assigned to them in infancy present a considerable problem. In developing countries, this problem is compounded by limited diagnostic and treatment facilities in addition to cultural, social, and religious problems which can dictate the management. Twenty-eight children with ambiguous genitalia were referred to or born at King Khalid University Hospital over a six-year period. Of these, 21 (75%) were Saudis and seven (25%) were non-Saudis. Nineteen (67.9%) had a positive relevant family history. Twenty-four (85.7%) were born in hospitals and four (14.3%) at home. In only three (10.7%) was the news broken to the parents by a senior doctor, in 13 (46.4%) by a junior doctor, and in 11 (39.3%) by a nurse. Ambiguous genitalia were suspected in 22 (78.6%) at birth and six (21.4%) were detected later. Thirteen (46.4%) had XX chromosomes, 11 (39%) XY, 1 (3.6%) XO, and chromosomal results were not available in 3 (10.7%). Congenital adrenal hyperplasia was the etiology in 14 (50%) of the cases, 5 α reductase in two (7.1%), and testicular feminization syndrome in five (17.9%), in addition to others. Of 22 cases observed at birth, sex was assigned without investigation in 19 (85.5%) of the cases. All were born outside King Khalid and lack of immediate investigative facilities was one of the main reasons for this. After investigation, five (17.9%) of the children needed sex reassignment. This was accepted in two cases and rejected for sociocultural reasons in three. The opinion of the religious leaders in these and other similar cases was obtained. Some recommendation on the handling of these cases is made based on local experience.

THE 3-HYDROXY 3-METHYL GLUTARYL (HMG) CoA LYASE DEFICIENCY: AN IMPORTANT CAUSE OF NEONATAL ORGANIC ACIDEMIA IN SAUDI ARABIA, A Al-Aqeel, H Gleispach, A Alodaib, G Gascon, M Nester, PT Ozand, King Faisal Specialist Hospital and Research Centre, and Riyadh Armed Forces Hospital, Riyadh

Neonatal organic acidemia caused by a deficiency of HMG CoA lyase is very rare; a recent review by Wyscoki and Hahn (J Inhert Metab Dis 1986;9:225) documents 19 cases in the world literature. The Inborn Errors of Metabolism Unit of King Faisal Specialist Hospital and Research Centre has nine cases in its files, suggesting that this disease is highly prevalent in the country. Four of these patients are under current management; one died late in infancy after considerable neurological damage had occurred and four others died neonatally following a severe and early onset of devastating metabolic disease of the newborn. The disease involves failure of leucine breakdown, resulting from deficiency of the enzyme at the last step of its metabolism (i.e., HMG CoA lyase). The accumulation of HMG CoA, following a diet containing leucine, or as caused by protein catabolism resulting from fasting or infections, causes severe and precipitous lactic acidosis, hypoglycemia, and hyperammonemia, which can lead to coma and death or neurological damage if there is not prompt intervention. The phenotypic expression of the disease can be varied; seven patients suffered severe lactic acidosis and hypoglycemia during the first 24 to 48 hours of life following the first feeding; two others did not manifest metabolic coma until 5 to 7 months of infancy. The disease can be successfully managed with dietary restriction of leucine, alkalinizing agents in the diet, and daily administration of L-carnitine. The patients who survived the initial metabolic coma are doing excellently with normal psychoneurological development and normal neuroradiological and neurophysiological findings. The disease can be diagnosed either by the characteristic organic acid excretion pattern in urine or by specific enzyme analysis in leukocytes and fibroblasts, which can be grown even from a postmortem skin biopsy. It is extremely important that this condition is considered in the differential diagnosis of any neonatal or infantile organic acid disorder in Saudi Arabia.

CHRONIC DIARRHEA IN THE RIYADH POPULATION, M Cheriyan, M Abanamy, H Salman, M Shuja, Suleimania Children's Hospital, Riyadh

Chronic diarrhea continues to be a major cause of significant morbidity in the pediatric practice. The management of children with chronic diarrhea is a challenging clinical problem which is highly rewarding in the vast majority. In this five-year retrospective review, 80 cases of chronic diarrhea were encountered at Suleimania Children's Hospital. The etiology, clinical presentation, investigations, and management strategies will be discussed. Rarer causes of chronic diarrhea, which include cystic fibrosis, ulcerative colitis, glucose–galactose malabsorption, and intestinal lymphangiectasia will be briefly discussed. Postgastroenteritis lactose intolerance (31%) and celiac disease (26%) were the most common causes of chronic diarrhea in this series. The mortality was 6%.

TWO-YEAR STUDY OF ACTIVE RETINOPATHY OF PREMATURITY FROM RIYADH ARMED FORCES HOSPITAL, SC Debnath, M Hasan, K Salamah, Riyadh Armed Forces Hospital, Riyadh

Retinopathy of prematurity (ROP) is a proliferative retinal vascular disease seen in low-birth-weight premature infants. It remains a problem in the visual development of such infants, despite the establishment of neonatal intensive care units. Most cases of ROP regress spontaneously. However, 10 to 20% progress. Cryotherapy has recently been found to be beneficial in stage 3 of active ROP. Since no such studies have been done in the Middle East, and especially in the Kingdom of Saudi Arabia, we started to examine such high-risk babies to allow for early detection and treatment of active ROP. Within a 2-year period, 60 high-risk infants were examined in our hospital. The modern classification, multiple high-risk factors, indication for cryotherapy, and our experience with ROP will be discussed.

THRYOID SCANNING AND PERCHLORIDE DISCHARGE TEST IN DETERMINING THE CAUSE OF CONGENITAL HYPOTHYROIDISM, M El-Desouki, N Al-Jurayyan, A Al-Nuaim, A Al-Swailem, King Saud University, King Khalid University Hospital, Riyadh

Congenital hypothyroidism (CH) can be caused by an absent or ectopic gland, or an inborn error of hormone metabolism. Determination of the etiology of CH is of genetic and prognostic importance. The aim of this study was to demonstrate the value of the thyroid scan and perchloride discharge test (PDT) in determining the cause of CH. Twelve neonates with CH were referred for thyroid scintigraphy. They were detected as the result of an ongoing neonatal screening program conducted at Ministry of Health hospitals in Riyadh. The 12 neonates were all born at term and were otherwise healthy. Their ages, at referral, ranged from 7 to 29 days (average, 12 days). Technetium 99m (TC-99m) thyroid scanning and PDT were performed prior to initiation of replacement therapy. Of the 12 patients studied, there were seven females and five males. The TC-99m thyroid scan revealed an athyrotic gland in four patients, ectopic gland in five, and goitrous gland in three patients. In seven of the eight patients with thyroid disease, PDT was performed and was positive in five (two ectopic and three goitrous thyroid). We conclude that thyroid scanning has a primary role in the evaluation of congenital hypothyroidism for detecting and localizing the thyroid gland and assessing uptake. When it demonstrates increased tracer uptake, dyshormonogenesis should be suspected and subsequently confirmed by PDT.

IGE RESPONSE IN CHILDREN TO VARIOUS ALLERGENS IN SAUDI ARABIA, AR Al-Frayh, MO Gad-El-Rab, SM Hasnain, College of Medicine, King Saud University, and King Faisal Specialist Hospital and Research Centre, Riyadh

Bronchial asthma in children is a common disease in Saudi Arabia, with up to 11.5% of the children, nationally, exhibiting wheezing. The disease frequency differs from region to region and extrinsic factors are considered important in the development of the specific IgE antibodies in susceptible individuals. Based on an aerobiological study, both indoor and outdoor, in Riyadh and other cities in the Kingdom, a panel of inhalant allergens was selected for skin prick test (SPT) to identify the causative agent. The panel included cockroach, cat and house dust mites, pollen, and fungi allergens, as well as cotton flock and horse epithelium, as miscellaneous allergens. SPT was conducted in a group of 55 asthmatic children (31 males, 24 females). Thirty-five allergens in total were tested, along with positive and negative controls. Thirty-five (63.7%) of the patients reacted to one or more allergens. Mild, moderate, and significant sensitivities were recorded for indoor allergens, pollen, fungal spores, and the miscellaneous group. The strongest reactions were recorded for indoor allergens. Twenty-eight positive reactions were recorded to differing fungi. The study indicates the association of various allergens in the IgE-mediated allergic disorders. Though some reactions were mildly positive, further investigation with more relevant and carefully selected allergens are necessary for the accurate diagnosis of the disease in the children of Saudi Arabia.

LYMPHSCINTIGRAPHY IN CHILDREN WITH LYMPHEDEMIA, M El-Desouki, King Saud University, King Khalid University Hospital, Riyadh

To overcome the potential side effects and difficulty in performing contrast-enhanced lymphangiography, radionuclide lymphscintigraphy was introduced in our department to evaluate patients with lymphedema. The procedure is simple, noninvasive, and does not require cannulation of the lymphatic vessels or injection of contrast material. To evaluate the diagnostic value of this procedure, we studied eight children with lymphedema. There were four males and four females, ranging in age from 2 months to 10 years. The procedure was performed by injecting 0.3 to 0.5 mCi technetium 99 antimony sulfide colloid (TL-99m ASC) intradermally into the first interdigital space bilaterally. Images of the lower extremities and pelvis were acquired using a large field of view gamma camera to demonstrate the lymphatic vessel and lymph node drainage of the lower extremities. The procedure was positive in all patients, demonstrating bilateral lymphatic obstruction in two, unilateral obstruction in five, and slow lymphatic flow in one patient. We concluded that lymphscintigraphy is a simple, safe, noninvasive, and highly accurate diagnostic imaging modality in the evaluation of lymphedema.

DIFFERENT TYPES OF METABOLIC WHITE MATTER DISEASES ENCOUNTERED IN SAUDI ARABIA, G Gascon, A Al-Aqeel, S Yamani, J Brismar, PT Ozand, King Faisal Specialist Hospital and Research Centre, Riyadh

Inherited white matter diseases primarily occur because of a specific inborn error of metabolism involving the synthesis of lipids or proteins by the myelin sheath, and can be caused by a metabolic disease of glial cells or abnormal peroxisomal structure. Secondary causes include metabolic defects involving amino acid metabolism and organic acidemias. The prevalence of the primary inherited leukodystrophies in the Kingdom will be presented. The Inborn Errors of Metabolism Unit at King Faisal Specialist Hospital has seen during the past 4 years seven patients with Austin's disease, a clinical condition which combines features of Maroteaux-Lamy syndrome and metachromatic leukodystrophy and is characterized by multiple sulfatase deficiency (MSD). The patients included four patients with metachromatic leukodystrophy (arylsulfatase "a" deficiency), one patient with globoid cell leukodystrophy (deficiency of galactosyl ceramide beta galactosidase), one patient with Zellweger syndrome (peroxisomal abnormality), and 16 cases of Canavan's disease. The defect in Canavan's disease is the absence of aspartoacylase, an enzyme that hydrolyzes N-acetyl aspartic acid, which presumably regulates the mitochondrial ion pump in glial cells. While a biochemical defect could be established in 29 patients, we have received 50 other cases in which no enzyme defect could be found. Three patients of the latter group might represent Pelizaeus-Merzbacher disease, and in five others, macrocephaly was associated with leukodystrophy, some of whom might have Alexander's disease. Most cases of unknown white matter disease were familial and involved both sexes. The pattern described in this report is significantly different from that observed in Western countries, since unknown causes, MSD, and Canavan's disease prevail, among others, in Saudi Arabia.

DIAPHRAGMATIC EVENTRATION: KING KHALID UNIVERSITY HOSPITAL EXPERIENCE, A Jawad, A Al-Rabeeah, AIY Al-Samarrai, King Khalid University Hospital, Riyadh

Eventration of the diaphragm is regarded as a rare problem in pediatric patients. It is classified into congenital or nonparalytic types and acquired or paralytic. Between 1987 and 1989, seven pediatric patients with diaphragmatic eventration were treated at KKUH. Their age ranged between 5 days and 5 years. Five had congenital diaphragmatic eventration and presented with repeated chest infections and dyspnea. The other two had an acquired diaphragmatic eventration following birth trauma, causing phrenic nerve and Erbs' palsy. One patient had an associated extralobar sequestration. The diagnosis was made on a clinical basis and confirmed by chest x-ray, fluoroscopy, and ultrasound of the diaphragm. Plication of the diaphragm was performed in all patients, using a thoracic approach in all, except two who had an abdominal approach. Two patients required short-term postoperative mechanical ventilation. One had diaphragmatic eventration, whereas the other had pneumothorax following abdominal-approach plication. All patients are alive and well on follow up. It appears that diaphragmatic plication is a safe and helpful procedure when performed for symptomatic pediatric patients with diaphragmatic eventration.

EPIDEMIOLOGY OF INTRAVENTRICULAR HEMORRHAGE IN PREMATURE INFANTS, S Khan, H Yaish, King Fahad National Guard Hospital, Riyadh

With the advent of modern perinatal care, increasingly immature infants are surviving. However, these extremely premature infants are prone to intraventricular hemorrhage (IVH) and all its potential complications. *Objective:* To determine the incidence, morbidity, and mortality related to IVH in an NICU population. *Methodology:* Infants admitted to the NICU with birthweight > 500 gm were eligible. The protocol required head ultrasound (U/S) screening of all infants less than 32 weeks' gestation and/or birthweight < 1500 gm. The U/S screenings were performed at 7 and 14 days of age. If IVH was detected, then weekly ultrasounds were performed until resolution of the IVH. *Results:* During the study period, 529 infants were eligible, of which 53 (10.1%) developed IVH. No significant differences were noted in the sex ratio, mode of delivery, or percentage of inborn versus transferred. The incidence of IVH was significantly lower in single versus multiple births (9.2 versus 16.9%; $P < 0.14$). Extremely low-birthweight infants (< 1 kg) accounted for 56% of IVH cases, whereas no cases were noted in infants > 2 kg. Infants on mechanical ventilation and BPD had a significantly higher incidence of IVH. Infants with IVH were hospitalized for twice as long as those without IVH (46 versus 23.5 days). Lastly, the mortality of infants with IVH was three times greater than that in the non-IVH group (37.7% versus 10.2%; $P < 0.001$). *Conclusions:* (1) the incidence and degree of IVH is inversely related to birthweight/gestation; (2) a significantly greater morbidity and mortality were noted in infants with IVH; and (3) advanced perinatal care has led to the survival of extremely immature infants, often with severe IVH. These infants may have a potentially poor neurological outcome, leading to a higher handicap rate.

CHILDHOOD HYPOTHYROIDISM: EXPERIENCE FROM THE KING KHALID UNIVERSITY HOSPITAL, RIYADH, N Al-Jurayyan, MA Abdullah, M El-Desouki, S Al-Habib, A Al-Nuaim, King Khalid University Hospital, Riyadh

Hypothyroidism is one of the most frequently encountered endocrine diseases in childhood. In Saudi Arabia there are no data on the prevalence of the disease; however, there is an impression fostered by clinical experience that it is not uncommon. We present our experience at the King Khalid University Hospital over the last 5 years. A total of 22 children with primary hypothyroidism were seen. Of these, two (9%) had Hashimoto thyroiditis and 20 (19%) had congenital primary hypothyroidism. In patients with congenital primary hypothyroidism, 17 (85%) were Saudi and three (15%) were non-Saudi. The mean age at diagnosis was 2.92 yr (range, 1 week to 9 yr). Female to male ratio was 1.5:1. Parents were related in 16 (80%) and family history was positive for hypothyroidism in 10 (50%). Radiological investigations were done in 16 (80%) of patients to identify the anatomical location and function of the gland. Of these, eight had dyshormonogenesis, six aplastic or hypoplastic, and two ectopic thyroid tissue. It is concluded that congenital primary hypothyroidism is not an uncommon disease with an increased prevalence of dyshormonogenesis in this group, which is probably due to the high rate of consanguinity among our population. Details of the clinical, laboratory, and radiological investigations will be discussed.

NEPHROTIC SYNDROME: SECURITY FORCES HOSPITAL EXPERIENCE, F Mansour, Security Forces Hospital, Riyadh

Nephrotic syndrome is a clinical entity with a variety of causes. It is characterized by increased glomerular permeability manifested by massive proteinuria. The pattern of glomerulopathy underlying nephrotic syndrome varies in different parts of the world. During the period from March 1985 until December 1986, 26 children presented with nephrotic syndrome or proteinuria in the nephrotic range. Age range of presentation was 6½ months to 13 years. All patients were Saudi except one (Egyptian). There were 11 females and 15 males. Twelve patients underwent kidney biopsy. The histopathological findings of these biopsy specimens were as follows: mesangeal proliferation, three; minimal change nephrotic syndrome (MCNS), two; focal glomerulosclerosis (FGS), one; membranoproliferative glomerulonephritis (MPGN), two; membranous glomerulonephritis (MGN), one; lupus nephropathy class II, one; Henoch-Schonlein purpura, one (the biopsy was inadequate); congenital nephrotic syndrome and diffuse mesangeal sclerosis, one. Two of the biopsy specimens were positive for HbsAg. The modalities of treatment and the outcome were discussed for some of the patients. It is difficult to determine the prevalence of certain underlying pathological conditions in nephrotic syndrome as the same patient may be seen in more than one institution. A registry for such patients would be particularly useful.

ESOPHAGEAL ATRESIA: KKUH EXPERIENCE, AM Khattak, A Al-Rabeeah, A Jawad, A Al-Bassam, AYI Al-Samarrai, King Khalid University Hospital, Riyadh

Between 1983 to 1989, 36 infants with esophageal atresia and/

or tracheoesophageal fistulae were seen at KKUH. Their weight ranged from 1020 to 3800 gm (mean, 2240 gm) and the sex distribution was equal. The average Apgar score was 5 in the first minute and 7 at five minutes. The diagnosis was made soon after birth in all but four, who were delayed 3, 5, 28, and 36 days, respectively. Eighteen patients (50%) had associated anomalies, ten of which were VATER associated. According to Waterston's risk classification, 19 children fell in group A, 4 in B, and 13 in C. Thirty-two infants had esophageal atresia with distal tetralogy of Fallot (TOF), three had H-type TOF, and one had an isolated atresia. Primary repair was performed in 31 infants; two had gastric and two colonic interposition. One infant is awaiting interposition. Follow up ranged from 6 months to 4 years (mean, 2 years). The postoperative complications included nine radiological leaks, five recurrent TOFs, and 12 anastomotic strictures. Two patients showed evidence of gastroesophageal refux. Four patients died (11%); three were from group C and one from group A. The survival is 94.7% for group A, 100% for group B, and 76.9% for group C. We attribute the mortality and morbidity in our patients to the associated anomalies and late referral of these patients. Our results are comparable to those reported in the literature; however, early diagnosis, early referral, and stabilization of the patient's condition before surgery will improve outcome.

INFANTILE POLYCYSTIC KIDNEY DISEASE: MCH, RIYADH EXPERIENCE, TK Mattoo, A Badr-El-Din, Y Katawee, M Ayman, AM El-Sowailem, Maternity and Children's Hospital, Riyadh

The study included ten patients (7M:3F) with infantile polycystic kidney disease (IPSKD). Age at the time of diagnosis ranged from 1 month to 7 years (median, 8 months). On admission, all were hypertensive and had palpable kidneys. Hepatic fibrosis with or without bile duct proliferation was seen in seven patients. A one-month-old baby died soon after admission, due to congestive cardiomyopathy. Two more neonates were lost to follow-up. The remaining seven were followed for 3 months to 3 years (mean, 18 months). All are normotensive on antihypertensive medication, and this includes one child who recently came off such therapy. In five patients the renal function either improved (N = 4) or remained stable (N = 1). Mild to moderate deterioration in renal function was seen in two patients; one (7 years) developed esophageal varices as well. Early diagnosis and appropriate treatment improves the prognosis of children with IPSKD, which until recently was considered to be a fatal illness.

MEASUREMENT OF INTRACRANIAL PRESSURE AND CEREBRAL PERFUSION PRESSURE IN FULL-TERM ASPHYXIATED NEONATES, NA Mir, S Javed, M Hassan, Institute of Medical Sciences, Kashmir, India

Asphyxia is one of the leading causes of perinatal mortality; the high degree of neonatal mortality and morbidity associated with this condition are related to the severity of hypoxic-ischemic encephalopathy (HIE) which is commonly associated with birth asphyxia. This study was undertaken to analyze quantitatively various pathophysiological changes in the cerebrovascular hemodynamics in HIE, and relate these changes to outcome. Eighteen full-term appropriate for gestation (AGA) infants (mean birth weight, 3234 g) with an Apgar score of < 5 were studied for continuous measurement of: transfontanelle intracranial pressure (Ladd ICP), arterial blood pressure (Doppler), and transcutaneous pO_2 and pCO_2, from birth to 72 hours of age. Intracranial hemorrhage (transfontanelle sonography) was excluded. Twenty-seven term healthy AGA infants (matched for birth weight and sex) served as controls. Six of the eight infants with cerebral perfusion pressure (CPP) < 20 died compared with one of the ten with CPP > 25. The study demonstrated that CPP is significantly reduced following birth asphyxia and a CPP of < 20 is indicative of poor outcome.

PRECOCIOUS PUBERTY: CLINICAL AND DIAGNOSTIC FEATURES, FM Mousa, AM El-Sowailem, EA Mikail, MF Salim, AA Jamil, Maternity and Children's Hospital, Riyadh

We describe 16 patients with precocious puberty seen at Maternity and Children's Hospital–Riyadh between 1984 and 1989. Nine patients were boys and seven were girls. Diagnosis of precocious puberty was based on: premature appearance of secondary sex characteristics, growth acceleration, and advanced skeletal age. The cause of precocious puberty was determined from basal and Gn-RH–stimulated gonadotropin level, pelvic and adrenal ultrasonography, computed tomography of the brain and abdomen, and levels of serum estradiol and testosterone, 17-OH progesterone, 11 deoxycortisol, and plasma ACTH. Of the nine boys, two had true precocious pseudopuberty (Tpp) due to brain tumor. Of seven boys with precocious pseudopuberty (ppp), five had congenital adrenal hyperplasia, one had adrenal carcinoma, and one had familial testotoxicosis, evidenced by enlarged testicular volume with low basal LH and FSH, prepubertal response to Gn-RH, high testosterone, and normal ACTH. Testicular biopsy was refused. Of the seven girls, four had Tpp with the following etiology: anomaly of central nervous system with convulsions (N = 1), idiopathic (N = 3). Three girls with ppp showed: ovarian cysts (N = 2) and congenital adrenal hyperplasia with simple virilization (N = 1). With advanced noninvasive techniques of investigations and available means for hormonal assay, it becomes possible to identify most organic causes of precocious puberty, and idiopathic causes should no longer be at the top of the list.

A PREVENTABLE DISEASE IN CHILDREN IN RIYADH, M Al-Mugeiren, AS Al-Rasheed, N Al-Jurrayan, PJ Patel, A Al-Boukai, College of Medicine, King Saud University, Riyadh

Vitamin D deficiency rickets was diagnosed in 55 children on the basis of clinical, biochemical, and radiological findings. Fifty-four (98.1%) were under 2 years of age. Seven children were diagnosed in the neonatal period. Twenty children were diagnosed in the first six months of life. Clinical findings of rickets were evident in malnourished as well as in well-nourished children. Convulsions were a presenting feature in 13 (23.6%) of the children. Recommendations to overcome this preventable disease were made.

SINUSITIS IN SAUDI CHILDREN, ZS Rafii, King Faisal Specialist Hospital and Research Centre, Riyadh

Sinusitis is considered one of the most common diseases in childhood, though no actual figures are quoted in the medical literature. This study which was conducted in an ambulatory care facility at King Faisal Specialist Hospital ans Research Centre in Riyadh, Saudi Arabia, a referral center for all Saudi Arabia, revealed a prevalence rate of sinusitis of 8.5% among new patients seen by the author over a 12-month period in 1988. The most common presenting symptom was cough (54%), while persistent rhinorrhea accounted for only 15% of the presenting symptoms. The most frequent predisposing factor was allergy (26%), followed by hypertrophied adenoids (25%) and septal deviation (13%). Other important factors, such as the low relative humidity in Riyadh, were also discussed.

URINARY TRACT INFECTION IN CHILDREN: WHY IS IT A PROBLEM?, M Al-Mugeiren, M Al-Oufi, PJ Patel, MB Abdurrahman, S Al-Rasheed, A Al-Boukai, College of Medicine, King Saud University, Riyadh

Urinary tract infection (UTI) is a common potentially serious pediatric problem. Underdiagnosis due to difficulties in recognition is frequent. In addition, those who are diagnosed are often underinvestigated. To improve the early diagnosis and thus prevent complications, we have reviewed our experience over five years (1403 to 1408). Eighty-one cases had proved UTI; 49 had probable UTI. Clinical, laboratory, and radiological findings will be described, and optimal diagnostic and therapeutic management as well as long-term follow-up will be suggested.

CONGENITAL HYPOTHYROIDISM: THE RKH EXPERIENCE OF THE LAST TEN YEARS, MA Majeed-Saidan, B Joyce, M Khan, H Hamam, Riyadh Armed Forces Hospital, Riyadh

The total number of infants screened from April 1985 til the end of December 1989 was 39,667. Sixteen children with congenital hypothyroidism were diagnosed, 15 in the neonatal period, 14 as part of the neonatal screening program (12 cord blood and two on-spot blood test at 7 days). This makes the incidence of congenital hypothyroidism in our screening program 1 in 2833 live births. The period of follow-up was between 3 months and 10 years; all patients seem to be normal both physically and intellectually. There are two families with more than one child affected, and one of twins. Eleven I^{131} thyroid scans were done; seven showed dyshormonogenesis and there was no thyroid tissue detected in four. Behavioral problems were noted in two children with normal development.

THE OUTCOME OF PERCUTANEOUS RENAL BIOPSY IN CHILDREN, SA Al-Rasheed, MM Al-Mugeiren, MB Abdurrahman, AT El-Idrissy, King Saud University, Riyadh

Although pediatric nephrology is a growing specialty in Saudi Arabia, there are no reports of percutaneous biopsy (PRB) carried out in children. We therefore decided to review the experience of PRB in children at King Khalid University Hospital over a 6½-year period. The objectives of the study were to analyze the indications, success rates, and complications of the procedure; to assess the feasibility of doing PRB in the Kingdom; and to compare our experience with that of workers in other parts of the world. One hundred twenty PRBs performed in 104 patients (aged 1 month to 15 years) were analyzed. Ultrasound was used for localization of the kidneys. Adequate renal tissue was obtained in 103 biopsies, with an overall success rate of 85.8%. The most frequent complication was gross hematuria, which occurred in 32 biopsies, but only five children required blood transfusion. Nineteen patients developed perirenal hematoma, which was symptomatic in two. Arteriovenous fistula was diagnosed in two patients. One patient died secondary to intestinal perforation. Serious complications were noted in patients with chronic renal failure. These results are comparable to the experience of renal biopsy in more developed countries. We conclude that PRB in children should be carried out in those centers where there is: (1) expertise for doing the procedure; (2) expertise for interpretation of the biopsies; (3) facilities for localization of the kidney; (4) facilites for complete evaluation of renal tissue (light microscopy, immunohistochemistry, and electron microscopy).

RESULTS OF TREATMENT IN PEDIATRIC NON-HODGKIN'S MALIGNANT LYMPHOMA, MF Salim, K Salamah, Maternity and Children's Hospital, Riyadh

Fifty cases of non-Hodgkin's malignant lymphoma were treated at the pediatric oncology section, MCH, Riyadh. Two different treatment protocols were used. The first did not include prophylaxis of the CNS while in the second intrathecal and intravenous methotrexate was administered to prevent CNS infiltration by the tumor. The second protocol also had a more prolonged induction period, though the drugs used (prednisolone, vincristine, cyclophosphamide, and adriamycin) were the same in both protocols. CNS prophylaxis reduced the incidence of meningeal relapse from 30% to 2% in the second group. In addition, the cure rate increased from 42% to 76% by use of a more aggressive induction and by the addition of intravenous methotrexate in the second group.

NEPHROTIC SYNDROME IN EARLY INFANCY: A CLINICOPATHOLOGICAL STUDY, SA Sanjad, EA Al-Sabban, M Akhtar, King Faisal Specialist Hospital and Research Centre, Riyadh

The clinical, laboratory, and histological data from eight patients with the nephrotic syndrome arising in the first 6 months of life were analyzed. All but one patient were seen over a consecutive three-year period ending December 31, 1989. This accounted for about 20% of nephrotics who underwent a kidney biopsy in the pediatric renal service at KFSH during this corresponding period. The onset of edema varied from 1 week to 5 months of age. The sex distribution was equal. Five of eight infants were born of consanguineous parents. One of the remaining three had a sibling who died with edema in early life. Four infants were born prematurely (28–32 wk). All had failure to thrive. Biochemical findings characteristic of the nephrotic syndrome were present in all patients. Alpha fetoprotein content was elevated in 5 of 7. TORCH titers were negative in 5 of 5. Three patients had evidence of renal tubular dysfunction characterized by glucosuria and renal bicarbonate wasting. Renal biopsy, performed in six patients, revealed focal segmental glomerulosclerosis in four, microcystic disease in one, and diffuse mesangial sclerosis in one. There were two hospital deaths, one from *E. coli* septicema, the other from pneumothorax. One patient is in partial remission, on diuretic therapy and angiotensin-converting enzyme inhibitor. The remaining five patients remained nephrotic for the length of their follow-up, which varied from 2 weeks to 6 months. *Conclusions:* (1) Nephrotic syndrome in the first 6 months of life is not infrequent in our experience. (2) Focal segmental glomerulosclerosis is the most common underlying pathology. (3) Long-term prognosis in this group of patients is guarded.

THE ROLE OF EXCHANGE TRANSFUSION IN THE MANAGEMENT OF CNS CRISIS IN SICKLE CELL DISEASE, K Salamah, MF Salim, Maternity and Children's Hospital, Riyadh

Seven percent of the patients with sickle cell disease are prone to brain infarcts as part of a vasoocclusive crisis. Repeat episodes during the subsequent year have been observed in 70% and patients frequently end as aphasic, double hemiplegics. These observations have been borne out by the experience in our center. A two-volume whole blood exchange transfusion was carried out in five children (ages, 9 months to 7 years) who presented with sickle cell CNS infarcts of recent onset. Three of these children had pre-existing neurological deficits from previous infarcts. All five cases were then started on a monthly hypertransfusion protocol to prevent recurrence. Dramatic improvement was noticed in two children treated for their first CNS crisis while the other three improved gradually to their pre-crisis state. Established brain infarcts cannot be reversed by this procedure but an exchange transfusion done early in the onset of the event can prevent serious and permanent CNS damage. Prevention of further episodes of CNS involvement seems possible by using a transfusion regimen intended to suppress the production of sickle cells over the following one year.

CURRENT MANAGEMENT OF CLEFT LIP & PALATE: SFH EXPERIENCE, ZA Skef, M Binshi, Security Forces Hospital, Riyadh

Cleft lip and palate are common among Saudi infants. An organized team approach in their management is essential to achieve good functional and cosmetic results. Newer trends emphasize the early anatomical correction of the defects and long-term follow-up. Family assurance and counseling are helpful. We reviewed our experience over a period of 30 months at the Security Forces Hospital. A total of 49 procedures were done in 39 patients. The average patient age of cleft palate repair was 10 months, and for cleft lip, 10 weeks. The male to female ratio was 29:10. There were associated anomalies in nine infants. Ten patients have had more than one surgical procedure; 37 children and infants underwent primary surgical repair at SFH, while all patients underwent revision because of unsatisfactory results from repairs done elsewhere. None of our primary cases has required any revision. Unilateral cleft lip was seen in 19 infants (female to male ratio, 5:14; right to left, 4:15). While a bilateral defect was present in 12 infants, ten were complete (female to male ratio, 3:9). Cleft palate was repaired in 17 infants (male to female ratio, 10:7). Incomplete cleft palate was present in nine. No operative mortality was encountered. One infant died 3 months postoperatively of complex cardiac defect, and another infant died at one year at home of possible aspiration and sudden infant death syndrome. Transfusion was needed in only one surgical procedure, of 49, because of preoperative anemia. Complications included two oronasal fistulae. It is too early to evaluate our speech results, but the impression is that early surgical repair of the palate (6–10 mo) was allowing a much better opportunity for speech development. This evaluation is under way now, and will be presented at a later time.

ACCIDENTAL POISONING OF CHILDREN IN RIYADH, SR Soliman, AM Al-Sowailem, Maternity and Children's Hospital, Riyadh

A retrospective study of 383 cases of poisoning seen at Maternity and Children's Hospital, Riyadh, during the Heijri year 1409 showed that 97% of the victims were four years or younger (age range, 3 months to 10 years). The ratio of Saudis to non-Saudis was 2.2:1 and male to female ratio, 1.5:1. Average hospitalization was 2 days. The mean duration of delay of arrival to hospital was 2 hours, the shortest was 15 minutes and longest, 12 hours. One child had two admissions because of poisoning. The poisoning agent included drugs in 263 cases, hydrocarbon in 68, chemical and household products in 40, and co-poisoning in 12 patients. Few attempts to induce vomiting at home using saline had been done, none using Ipecac. No symptoms were seen in 51.5% of cases, 36% had mild to moderate symptoms, and 12.5% had severe symptoms. There were no deaths. This study is preliminary and a prospective study is planned. Prevention of poisoning requires adequate knowledge of the hazardous properties of substances and this requires education through the media about safe storage and handling. Physicians when prescribing drugs should be alert to their toxicity and instruct parents accordingly. The effectiveness of child-resistant closures has reduced the incidence of ingestion by 40 to 50%. A regional poisoning control system to help parents over the telephone can help reduce the number of admissions and morbidity. There is a center of information for medical personnel inquiry at King Khalid University Hospital in Riyadh.

IMAGING STRATEGIES IN PEDIATRIC LEUKOENCEPHALOPATHY: MR VERSUS CT, L te Strake, J Brismar, R Coates, G Gascon, PT Ozand, A Haider, W Greer, King Faisal Specialist Hospital and Research Centre, Riyadh

The purpose of this study was twofold: to compare MRI and CT in the detection of white matter disease (WMD) and to study the efficacy of different conventional spin echo (SE) and rapid gradient echo (contrast-enhanced FAST, CEFAST) MRI techniques. During a 16-month period (May 1989 to September 1989), 96 patients were found to have WMD on MRI. In 51 patients, CT was performed within 2 months before or after MRI, and a statistical comparison was made between MRI and CT for detection of WMD. Thirty-six patients were older than 12 months, and 15 patients were less than 12 months of age. Twelve areas of the brain were assessed and scored as positive, negative, or uncertain for the presence of WMD. In patients older than one year, the differences between MR and CT were statistically highly significant; in 44% of the patients with positive WMD on MRI, CT was considered negative or uncertain. No statistical difference was found in the age group less than 12 months. In patients with immature brain, it is difficult to reliably distinguish between normal and abnormal white matter. CEFAST was performed in 50 patients and compared with a conventional SE pulse sequence. CEFAST was considered useful for monitoring focal changes of white matter in the neonatal brain and for enhancing differences in normal and abnormal white matter in infants under 6 months of age. In two children over 1 year of age, CEFAST detected more extensive WMD than did the conventional SE technique.

MANAGEMENT OF IDIOPATHIC THROMBOCYTOPENIC PURPURA IN CHILDREN: IMMUNOSUPPRESSION OR IMMUNOPROTECTION?, H Yaish, King Fahad National Guard Hospital, Riyadh

We describe the clinical course observed in 104 children with idiopathic thrombocytopenic purpura (ITP) who were referred to our service over a period of 5 years. Ninety-five children (48M:47F), ranging in age from 4 to 192 months, were eligible for this study, which was designed to evaluate the efficacy of corticosteroids in the management of ITP. Children who presented within 2 weeks of onset and who were judged to be at high risk of serious bleeding were submitted to a course of corticosteroids (N = 27). None were over 10 years of age. Children 10 years of age or younger who presented within two weeks of onset and who received no corticosteroid therapy served as the control group (N = 120), representing the natural course of the disease. The earliest significant increase in platelet count was evaluated to allow comparison of the cumulative proportions in each group achieving appreciable elevations of platelet count (25,000/m^3 or more) on each of the first 21 days after onset. At nine days after onset, the difference between the proportions of the treated and untreated patients achieving such elevations became statistically significant ($P < 0.05$). Patients with chronic ITP who failed to respond to corticosteroid therapy also failed to respond to either azathioprine or cyclophosphamide, with or without corticosteroids. Seven patients with chronic disease who had responded to corticosteroids initially subsequently relapsed, but all responded to a second course of corticosteroids, though none sustained remission. Four children received high-dose IV immunoglobin; one failed to respond and remission developed in three, two required maintenance therapy for several months. We conclude that corticosteroid therapy in children considered at increased risk of hemorrhage resulted in a significantly greater number of patients with an early increase in platelets than was noted in the control group. We also found that children with chronic ITP who failed to respond to immunosuppressive therapy have frequently shown dramatic response to high-dose IV immunoglobin.

CHILDHOOD BRUCELLOSIS IN KUWAIT: A PROSPECTIVE CLINICAL AND LABORATORY STUDY OF 402 CASES, MM Lubani, GF Araj, Q Al-Saleh, TS Al-Shab, DC Sharda, M Al-Mutairi, I Al-Shami, A Nasrallah, Farwania Hospital, Faculty of Medicine, Kuwait Univesity, Kuwait

Brucellosis is regarded as uncommon in the pediatric age group. Over the last 3 years, we prospectively studied the clinical pattern and laboratory findings in 402 consecutive children with brucellosis. Patient age ranged from one hour to 14 years (mean, 7.2 yr) and the male to female ratio was almost 1.1. The source of infection was raw milk ingestion in 54% of the cases. The main presenting clinical features were fever (91%), arthralgia (65%), weakness/fatigue (56%), arthritis (30%), weight loss (27%), and hepatosplenomegaly (26%). Other less frequent findings included cough, vomiting, chills, low back pain, insomnia, depression, anxiety, coma, convulsions, and lymphadenopathy. The hemogram showed leukocytosis (in 14% of the patients), leukopenia (13%), lymphocytosis (83%), thrombocytopenia (5%), and pancytopenia (1%). The ESR was < 50 mm/1 hr in 96% of the patients. Elevated liver enzymes (ALT, AST, LDH) were found in 65% of the patients. Among the brucella-specific tests, ELISA provided the most reliable results, being positive for IgM alone or together with IgG and IgA in all patients. Brucella culture was positive in 47% of the cases, the organisms being *B. melitensis* in all. Brucella complications included hepatitis (5% of the cases), neurological (2.2%), renal (2.2%), pulmonary (1.2%), pancytopenia (1.2%), osteomyelitis (0.7%), and myocarditis and endocarditis (0.7%). Treatment with either oxytetracycline, doxycycline, or rifampicin gave a cure rate of 90%. Cotrimoxazole (TMP/SMX) alone was associated with a high relapse rate (42%). Generally, improvement in clinical condition was observed within one week of starting therapy. We recommend a combination of TMP/SMK (10/50 mg/kg/day orally for 3 weeks) along with intramuscular gentamicin (5 mg/kg/day) over the first five days in children < 8 years and for children > 8 years, oxytetracycline (20 mg/kg/day) or doxycycline (5 mg/kg/day) over 3 weeks, along with gentamicin over the first five days of the illness. Thus the incidence of brucellosis in children seems high in areas around the world where the disease is still not eradicated and the diagnosis of brucellosis should be considered in the differential diagnosis of fever of unknown origin in children from these areas.

IMMUNOGENICITY OF HEPATITIS B VIRUS VACCINE IN SAUDI NEONATES, HT Tufenkeji, FN Takieddine, MH Ghandour, King Faisal Specialist Hospital and Research Centre, Riyadh

Over the past 6 years, the immunogenicity of hepatitis B virus vaccine was studied in 102 Saudi neonates born to hepatitis B surface antigen–positive mothers. Neonates received hepatitis B immune globulin and the first of a 10 μg dose of vaccine shortly after birth. Two additional doses were given at 2 and 6 months. By the age of 8 months, 99 (97%) of the vaccinees had detectable anti-HBs in their serum, indicating immunity, and 48 (47%) had anti-HBc which was probably passively acquired. Two of the three who did not have anti-HBs after three doses did respond to a fourth dose. None of the infants developed hepatitis B surface antigenemia. Hepatitis B vaccine is highly immunogenic in Saudi infants, but duration of immunity and efficacy will require further studies.

NEUROLOGICAL AND NEUROPSYCHOLOGICAL DYSFUNCTION AS A RESULT OF DEPRESSION AND MANIC-DEPRESSIVE DISORDERS IN CHILDREN: AN UNDERRECOGNIZED CAUSE OF LEARNING DISABILITY AND SCHOOL FAILURE, RA Brumback, University of Oklahoma, Oklahoma City, Oklahoma, U.S.A.

Epidemiological studies suggest that 5% of all office visits to pediatricians are for behavioral or learning problems, and school surveys suggest that 30% of school age children are affected by learning disabilities. Depression is the most common cause of chronic or recurrent school problems with or without learning disabilities in otherwise healthy, normally intelligent young people. The clinical symptoms of depression can generally be divided into two categories: psychological and physiological. Changes in psychomotor activity (either increased or decreased) and a reduction in motor proficiency are also apparent. Biochemical alterations in the brain that accompany depression or mania can produce widespread alterations in cerebral functioning, and associations between neurological signs of cerebral dysfunction and depression are well recognized. The relationship of depression and right cerebral dysfunction probably explains the poor short- and long-term academic performance and social adjustment found in studies of depressed children. In discussion of learning disabilities, there is an emphasis on left cerebral language functions, even though other hemispheric specializations are equally important. The right hemisphere is dominant for behaviors and activities that permit socialization and functioning in independent interactive individuals. Current research indicates that depression is a form of metabolic encephalopathy resulting from an episodic disturbance of the aminergic neurotransmission which modulates cerebral neuronal activity. Insufficient antidepressant therapy with resultant intermittent depression-induced dysfunction of the socialization functions performed by the right cerebral hemisphere would not permit the child to develop appropriate interpersonal skills, while associated cognitive difficulties would complicate academic performance. Repeated school failure and chronic social ineptitude preclude development skills necessary for successful independent living in society. Thus, if symptoms of depression are found, adequate antidepressant therapy must be instituted to ensure complete long-term remission of the depression. In addition, learning-disabled individuals must be offered appropriate methods for learning and communication which reduce stress. The depressive nature of symptoms may not become apparent until treatment-induced improvement has occurred and depression-associated learning disability has resolved. Improved academic performance can be dramatic with resolution of the apparent learning disability.

DISORDERS IN THE SPECTRUM OF AUTISM: KING FAISAL SPECIALIST HOSPITAL SERIES, MJ Nester, GG Gascon, PT Ozand, King Faisal Specialist Hospital and Research Centre, Riyadh

The spectrum of autism is broad and includes infantile autism, Rett's syndrome, pervasive developmental delay, and others. In the Kingdom of Saudi Arabia, it is not well delineated. We have followed 22 patients that fall within this area during 1988 at KFSH. The demographic aspects of these patients, as well as findings of special interest, were discussed. These include the issues of consanguinity, a positive family history, CT, and EEG findings. Patient characteristics were compared to those seen in the West with similar diagnoses. Concerns related to difficulties in treatment and educational placement are considered, along with future directions within the Kingdom.

MYOTONIC DYSTROPHY: A DISEASE OF ABNORMAL MEMBRANE RECEPTORS, RA Brumback, University of Oklahoma, Oklahoma City, Oklahoma, U.S.A.

Myotonic dystrophy (Steinert's disease) is the most common inherited neuromuscular disorder. It is characterized by myotonia and progressive distal weakness. There are also associated behavioral symptoms of apathy, reduced initiative, moodiness, and suspiciousness. Brumback and co-workers have described myotonic dystrophy patients as having high scores on the Hamilton Rating Scale for Depression, fulfilling DSM-III criteria for a major depressive disorder, and showing a depressive profile on the MMPI. Imipramine has been observed to be effective in managing both the muscular disability and depression in such patients. Based on reports of a variety of membrane receptor disturbances in myotonic dystrophy patients, Brumback and co-workers hypothesized that the symptoms may be caused by a generalized deficiency of aminergic and peptidgeric receptor function. The finding of biological depressive illness indicated abnormality of central nervous system catecholaminergic and/or serotonergic receptors. Myotonia can be exacerbated by the β-adrenergic antagonist propranolol and improved by the β-adrenergic agonist albutamol. According to the hypothesis that explains the muscular defect of myotonic dystrophy in terms of deficient β-adrenergic inhibition of myofiber excitability, B-adrenergic (agonist) stimulation should alleviate myotonia only to the extent it exerts an inhibitory influence on skeletal muscle. One beneficial effect of β_2-adrenoreceptor stimulation in myotonic dystrophy could be an induced increase in electrogenic Na^+-K^+ pump activity. More generally, it seems probable that the beneficial effect of imipramine in patients with myotonic dystrophy is to augment the hyperpolarizing and inhibiting effects of β_2-adrenoreceptor stimulation of skeletal muscle membranes. Imipramine may act on sympathetic nerve terminals within muscle tissue to increase perivascular levels of norepinephrine which exert a paracrine, inhibitory (modulatory) influence on muscle membranes.

Poster Presentations

VARIANTS OF ATAXIA TELANGIECTASIA IN SAUDI ARABIA, G Gascon, M Hannan, M Waghray, H Harfi, K Sheth, M Nester, E Rabe, King Faisal Specialist Hospital and Research Centre, Riyadh

We have investigated two families with five affected members exhibiting true ataxia telangiectasia who showed the full spectrum of ataxia, oculomotor apraxia, and telangiectasia, with increased serum alpha fetoprotein and chorioembryonic antigen contents, decreased serum immunoglobulin levels, defective blastogenesis or mitogen stimulation assays, increased chromosomal breaks on acute radiation (other one patient showing a heretofore unreported 7,14 translocation), and increased sensitivity of cultured fibroblasts to radiation. In addition, we have identified the following phenotype variations, with supportive laboratory characteristics, or what we call "clinical variants of ataxia telangiectasia."

Clinical diagnosis	No. of patients	Laboratory results	
Ataxia-oculomotor apraxia syndrome	3	↓ Blastogenesis	= 3
		↑ Chromosome breaks	= 1
		↑ Radiation sensitivity	= 3
Ataxia with recurrent infections	3	↓ IgA = 2, ↓ IgM	= 1
		↑ Chromosome breaks	= 1
		↑ Radiation sensitivity	= 1
Telangiectasia without ataxia	2	↓ IgE = 1, ↓ IgM	= 1
		↓ Blastogenesis	= 1
		↑ Chromosome breaks	= 1
		↑ Radiation sensitivity	= 1

We propose that these variants may exist unrecognized in the Saudi population, and may be clinically important because of the known high incidence of cancer, particularly lymphoma and leukemia associated with homozygotes and heterozygotes of ataxia telangiectasia.

EMPTY SELLA SYNDROME IN CHILDREN: ITS RELATIONSHIP WITH INCREASED SELLA SIZE AND ENDOCRINE DISTURBANCE, L Garcia, A Akkad, King Fahad National Guard Hospital, Riyadh

When arachnoid-containing CSF herniates into the pituitary fossa and compresses the hypophyseal gland against the floor of the sella turcica, it creates the illusion of an "empty sella." In adults this condition is relatively common. Autopsy studies revealed that 5 to 23% of the adult population have empty sella (ES) and/or an incompetent sellar diaphragm. The great majority of cases of ES in adults have a big sella without bone changes. ES may be primary (without apparent reason) or secondary, following sellar region surgery or radiotherapy. Empty sella in children has received little attention in the medical literature, and up to 1983, only 27 cases were reported. In the last 6 years, several reports have stressed the differences that exist compared with adult series. In children, the sella is normal sized in most cases and ES is rarely found as a cause of an enlarged sella, being 1% in one series of 360 cases of big sella in children. Children with ES are not obese, and there is no sexual preponderance. The incidence of endocrine (pituitary-hypothalamic) dysfunction is much higher in children with ES (25 to 50% of cases), probably due to the selected studied population. Endocrine abnormalities seem to be more common in patients with normal-sized sella than in those with large ones for both adults and children. ES has been found in up to 24% of a selected pediatric population (with growth retardation or suspected endocrine dysfunction). Diagnosis of ES used to be done with air studies (pneumoencephalogram) and since 1980 by computed tomography. We present a case of ES in a 6-year-old child who had ES with a big sella and growth retardation, with normal endocrine function. The true incidence of ES in children is unknown but magnetic resinance imaging resonance imaging will probably help identify the real incidence of this condition in children as well as in adults.

HYPOMELANOSIS OF ITO (INCONTINENTIA PIGMENTI ACHROMIANS): SPECTRUM OF DISEASE, S Hassan, A Jamil, N Barkouny, AM Al-Sowailem, S Kinani, Maternity and Children's Hospital, and Riyadh Central Hospital, Riyadh

Hypomelanosis of Ito (HI) described first by Ito (1952) is an uncommon neurocutaneous syndrome encountered in the pediatric clinical practice. The clinical spectrum observed over the years by various authors includes obligate neurodevelopmental delay, bizarre hypopigmented skin lesions (either linear and/or whorls), squinted eyes, and kyphoscoliosis. There are some rare associations such as malignant hypertension [Pediatrie 1986;41(7):565-70], insulin-dependent diabetes mellitus [Ann Acad Med Singapore 1985;14(2):317-9], thyroid dysfunction (goiter) [Ann Acad Med Singapore 1985;14(2):317-9], heterotopias of the gray matter shown by MRI [Magn Res Imaging 1986;4(1):33-9], and hepatosplenomegaly. Rarely chromosomal aberrations (e.g. mosaicism or chimerish or chromosomal abnormalities [Lancet 1986;2(8502):343] are also reported. Etiopathogenesis of HI remains obscure. The inheritance pattern is also unclear. Family studies indicate the effect of a single mutant gene but whether it is autosomal or x-linked remains to be determined. This calls for a close examination of parents and genetic counseling. The present paper includes a report of two unrelated cases (both males), aged 9 months and 7½ years, admitted to MCH, Riyadh, with developmental delay and cutaneous manifestation (linear whorls, and spirals of hypopigmented lesions) with squint and epilepsy. Analysis of the clinical manifestation and neurodevelopmental aspects will be highlighted. This paper emphaiszes the need for special attention in cases referred for neurodevelopmental assessment.

GENETIC DISORDERS IN THE PEDIATRIC AGE GROUP: ONE-YEAR EXPERIENCE OF THE GENETIC UNIT AT THE CENTRAL LABORATORY AND MATERNITY AND CHILDREN'S HOSPITAL (MCH), RIYADH, MO EL-Ruby, AH Choudhury, A El-Derees, AM El-Sowailem,Central Laboratory and Blood Bank, Riyadh

We have investigated 704 pediatric cases (361 females and 343 males) referred to the genetic unit of the central laboratory for chromosomal analysis and genetic counseling in the year 1409H. We classified the cases into four age groups: neonate (310 cases), infancy (156), toddler (185), childhood (113), and adolescent (40). Most cases were referred from the Riyadh area (541 cases, 77%) and the remaining 163 cases (23%) were from other areas of the Kingdom. From the Riyadh area, 48% of the cases were from MCH, 20% from Solimania Hospital, 10.5% from Prince Salman Hospital, 10.2% from Yamamah Hospital, 5.2% from Riyadh Central Hospital, and the remaining 6.4% were from other centers and dispensaries. Chromosomal analysis and full genetic evaluation were performed and chromosomal aberrations were diagnosed in 185 cases (26.3%), of which 21 trisomy was the most frequent (131 cases). Other chromosomal abnormalities included 54 cases, of which 13 trisomy, 18 trisomy, and other rare autosomal abnormalities were documented as ring 18, 18p-, 13q-. Among the sex chromosomal aberrations, 45XO, 47XYY, 48XXYY, FRAG.X syndrome, and testicular feminization syndromes were diagnosed. Some known dysmorphic syndromes of normal chromosomal constitution were also documented and diagnosed (29 cases), including Prader Willi, Laurence Moon, Biedl, Goldenhar, xeroderma pigmentosa, Noonan, Russell Silver, Seckel, prune-belly, and others.

NONKETOTIC HYPERGLYCINEMIA: A DIAGNOSTIC AND THERAPEUTIC PROBLEM IN EARLY INFANCY, AA Jamil, SR Soliman, AM Al-Sowailem, Maternity and Children's Hospital, Riyadh

Nonketotic hyperglycinemia (NKH) is an inborn error of amino acid metabolism in which large amounts of glycine accumulate in body fluids and subsequently organic acids cannot be demonstrated in the blood or urine by screening. This fact differentiates it from ketotic hyperglycinemic syndromes like propionic acidemia, and other disorders of organic acid metabolism. NKH was first described in detail by Gerristen et al in 1965. It is a relatively frequent metabolic cause of devastating illness in the neonatal period with refractory convulsions. The basic metabolic defect lies in the slower or decreased glycine cleavage system, which is entirely mitochondrial, and is due to abnormal P&T protein moities. NKH is probably heterogeneous with an autosomal (recessive) pattern of inheritance. There are two recognized clinical types of NKH: a typical form occurs as a classic overwhelming life-threatening disease in the neonatal period in the form of apnea, feeding difficulties, and seizures which do not respond to conventional anticonvulsants; an atypical NKH occurs as a mild syndrome leading to significant psychomotor retardation with and without epilepsy and is of late onset. The survivor of classic NKH has intractable predominantly myoclonic seizures. No effective treatment, curative or symptomatic (anticonvulsant), has been consistently reported. However, sodium benzoate, strychnine, diazepam, and dialysis (PD & HD) have been tried as possible therapeutic modalities with no encouraging outcome. This presentation includes three cases of intractable seizures admitted to Maternity and Children's Hospital, Riyadh (in 1409 H). Data analysis of these cases was presented, with a brief review of the literature. All neonates and young infants who have intractable convulsions should have a thorough and early neurometabolic work-up.

UNUSUAL PRESENTATIONS AND COMPLICATIONS OF SALMONELLA ENTERITIDIS IN CHILDREN, NM Soliman, AM Al-Sowailem, Maternity and Children's Hospital, Riyadh

We report on three patients who had normal hemoglobin levels and no demonstrable immunological abnormalities. Two are siblings who presented wtih generalized lymphadenopathy and hepatosplenomegaly. Both suffered cervical lymph node abscesses, which required surgical drainage. *Salmonella enteritidis* group C was grown from the pus, blood, and stool of these patients. One of the siblings developed purpuric rashes on the lower limbs similar in character and distribution to the rash of Schonlein-Henoch purpura. The same organism was grown from stool of their mother, who was found to have gallbladder stones and who subsequently underwent cholecystectomy. The third patient presented with purpuric rashes on both upper and lower limbs which was diagnosed as Schonlein-Henoch purpura with recurrent relapses because of the typical distribution and character of these rashes. After the second relapse, the child was noticed to have generalized lymphadenopathy and hepatosplenomegaly. Each time, *Salmonella enteritidis* group B was cultured from his blood and stool, but the coagulation profile was always normal. *Salmonella enteritidis* infections are usually brief and self-limiting, and confined to the bowel unless there is alteration of the local protective mechanisms or impairment of the immune system. Abscesses and vasculitis do occur due to *Salmonella enteritidis* but are very rare. No similar reported presentations and complications could be traced in the Saudi medical literature. It is hoped that drawing attention to these cases will alert clinicians to the existence of such cases, as the prevalence and clinical significance of invasive salmonellosis due to nontyphoidal salmonella are often not appreciated.

COMBINATION THERAPY OF SSPE WITH ISOPRINOSINE AND ALPHA INTERFERON, S Yamani, G Gascon, A Cafege, King Faisal Specialist Hospital and Research Centre, Riyadh

We treated two patients with subacute sclerosing panencephalitis (SSPE) using combined oral isoprinosine (100 mg/kg/day PO in divided doses) and intraventricular alpha interferon, a combination not yet reported in the world literature. Both patients entered the hospital in stage II, but their condition rapidly deteriorated to stage III despite oral isoprinosine. Therefore, an Ommaya reservoir was surgically installed over the right anterior skull, and 500,000 to 1,000,000 units of alpha interferon was instilled twice weekly. Patient 1's condition stopped deteriorating within 10 days, plateaued, and then began to recover [neurological disability index scores decreased from (48 ± 3)/80 to 36 ± 3)/80 over 6 weeks]. However, there was no further recovery after 3 months. On the same treatment, Patient 2's condition steadily deteriorated after 6 weeks of combination treatment, and therefore it was discontinued. A pilot study is under way to determine whether such combination therapy would be worthwhile extending to multicenter clinical trials.

SERIOUS SERRATIA OUTBREAK IN A BUSY PEDIATRIC UNIT, YT Oke, MA Chowdhury, King Khalid Hospital, Najran

We report a serious outbreak of *Serratia* infection in our busy pediatric ward. Eleven infants were affected, six with gastroenteritis, four with bronchopneumonia, and one with a history of kerosene ingestion causing severe bronchopneumonia. Two patients died. Overcrowding, mixing of IV fluids, and keeping the IV cannulae in place for more than 48 hours were some of the factors responsible for this outbreak. We discussed the *Serratia* infection in general and suggested certain measures that are absolutely necessary to prevent such an outbreak in the future.

FANCONI ANEMIA: PROLONGED REMISSION WITH CORTICOSTEROIDS AND ANDROGEN THERAPY—A CASE REPORT, SR Soliman, AM Al-Sowailem, Maternity and Children's Hospital, Riyadh

Two siblings of a Saudi family presented with pancytopenia, delayed development, short stature, skeletal changes, skin hyperpigmentation, hypogenitalism, congenital kidney malformations, and chromosome breaks. Two other siblings were normal. Preliminary treatment with corticosteroids and androgens resulted in remission with a gain in height and weight, abatement of pancytopenia, and cessation of the need for blood transfusions. Fanconi anemia is inherited as an autosomal recessive disorder with multiple symptomatology, pancytopenia, chromosome breaks, and increased susceptibility for malignancy.

FAMILIAL MEDITERRANEAN FEVER, N Barkouny, S Hassan, AM Al-Sowailem, Maternity and Children's Hospital, Riyadh

Familial Mediterranean fever (FMF) is an uncommon disease in Saudi Arabia, and in children it is not easily diagnosed. It was described for the first time by Janeway and Mosenthal in 1908. FMF is a cyclic inflammatory disease of unknown pathogenesis and autosomal recessive inheritance. The clinical spectrum is characterized by recurrent episodes of fever, peritonitis or pleuritis, arthritis, skin lesions, and amyloidosis. It is associated with severe myalgia [Ann Rheum Dis 1988;47(1):80-3], acute orchitis [Ann Intern Med 1988;109(2):164-5], polyarteritis nodosa [Br J Rheumatol 1987;26(2):139-41], increased procoagulant response of monocytes [Thromb Haemost 1986;56(2):211-3], episcleritis [Ann Ophthalmol 1985;100(2):337-9], C5a-inhibitor deficiency in peritoneal fluids [N Engl J Med 1984;311(5):325-6,287-90], and defective suppressor cell function [Clin Exp Immnol 1981;43(2):357-61]. Metaraminol provocation test specific diagnostic test for FMF [Lancet 1984;1(8378):656-7]. The etiology of this disease is not clear but abnormalities in catecholamine metabolism may be a factor. Diagnosis of FMF is often difficult and based on precise clinical criteria and genetic disorder (A-R). It is more frequently seen in persons of Mediterranean descent. Diagnosis of FMF has also been one of exclusion but the metaraminol provocation test (10-mg infusion) followed within 48 hours by a typical disease-like attack, which is prevented by colchicine, is of use in determining diagnosis. This paper included a report of two cases admitted to the RMCH with a typically long history of recurrent episodes of fever, abdominal pain, chest pain, arthritis, skin lesions, and positive family history and proved by metaraminol provocation test and improved with colchicine (0.5 mg 12 hourly), followed up regularly without any complication from either disease or drug. The diagnosis of FMF is too often missed in pediatric practice.

NEONATAL CHYLOUS ASCITES EXPERIENCE AT KING KHALID UNIVERSITY HOSPITAL, A Al-Bassam, A Ali, A Alrabeeah, Y Alissa, M Ahmed, King Khalid University Hospital, Riyadh

Neonatal chylous ascites is a rare condition. Over 60 cases occurring in neonates and children have been reported in the literature. We report four cases of neonatal chylous ascites referred to KKUH during the last two years. All patients were below the age of 7 months, two were males and two were females. Two were siblings. All cases were referred from outside the hospital. The main presentation was abdominal distention since birth. In addition, two presented with diarrhea. The diagnosis of chylous ascites was confirmed by jejunal biopsy. A major lymphatic leak was found at laparotomy in one patient. All patients were treated conservatively with a high-carbohydrate, high-protein, median chain-triglyceride diet. Two had laparotomy, and a correctable cause was found in one. One patient died because of cardiorespiratory failure and malnutrition. The other two are still under conservative treatment. In conclusion, most cases of neonatal chylous ascites have no underlying surgical cause and a good number will respond to conservative management in the form of dietary manipulation. However, should a surgical cause be found or medical therapy fail, surgical exploration may prove to be beneficial.

Announcements

The *Annals of Saudi Medicine* is pleased to publish announcements of educational opportunities of interest to its readers. For adequate publicity, notices of postgraduate courses, meetings, and lectures must be received at least 6 months before the date of occurrence. Please send relevant information to the *Annals of Saudi Medicine*, Publications Office, King Faisal Specialist Hospital and Research Centre, P.O. Box 3354, Riyadh 11211, Saudi Arabia.

King Saud University Fellowship in Pathology

King Saud University announces the inception of a 5-year joint fellowship training program in pathology. The training will be at King Khalid University Hospital, King Faisal Specialist Hospital and Research Centre, and Riyadh Armed Forces Hospital, and is a full-time program. Application is open to interested and suitably qualified residents from all over the Kingdom. To be eligible, applicants will meet the following criteria:

1. Doctors who hold MB,BS from King Saud University or equivalent degree with at least Good grade.
2. Doctors who have finished their internship in a recognized hospital with at least a Very Good grade.
3. Successful completion of a selection examination and personal interview.
4. Applicants from other institutions should submit a letter from his/her employer that he/she will be sponsored during the whole period of training.

Applications and inquiries should be sent to the Director, Postgraduate Medical Education, College of Medicine, King Saud University, P.O. Box 2925, Riyadh 11461, Saudi Arabia.

King Faisal Specialist Hospital and Research Centre Postgraduate Training Programs

King Faisal Specialist Hospital and Research Centre is pleased to invite applications for the following full-time postgraduate training programs:

1. Arab Board residency training in the specialties of internal medicine, obstetrics/gynecology, pediatrics, and surgery.
2. Five-year pathology residency training program, affiliated with the Royal College of Pathologists of Australasia and the King Saud University.
3. Fellowships, both adult and pediatric, in cardiology, endocrinology, gastroenterology, infectious diseases, nephrology, hematology, and oncology. Also, adult pulmonary and critical care medicine, adult rheumatology, pediatric allergy and clinical immunology, neonatal/perinatal medicine, and pediatric neurology.

For further information contact the Director, Academic Affairs and Postgraduate Education, King Faisal Specialist Hospital and Research Centre, P.O. Box 3354, Riyadh 11211, Saudi Arabia; telephone (01) 464-7272, extension 1837.

Radiopharmaceuticals from King Faisal Specialist Hospital and Research Centre

King Faisal Specialist Hospital and Research Centre manufactures various radiopharmaceuticals at its Radionuclide and Cyclotron Operations facility with the aid of model CS-30 Cyclotron. These radiopharmaceuticals are produced according to international standards of good manufacturing practice. The Research Centre meets the high standards of quality assurance and environmental safety with regard to radiopharmaceuticals.

Radiopharmaceuticals currently produced and available for distribution throughout the Kingdom and to adjoining Arab states are as follows: thallous (Tl-201) chloride injection ($T^{1}/2$ = 73 h); gallium (Ga-67) citrate injection ($T^{1}/2$ = 78.3 h); iodine-123 capsules ($T^{1}/2$ = 13.1 h); iodine-123 oral solution ($T^{1}/2$ = 13.1 h); iodine-123 orthoiodohippurate solution ($T^{1}/2$ = 13.1 h); rubidium (Rb-81) → krypton (Kr-81 m) generator ($T^{1}/2$ = 4.58 h – 13 s); indium (In-111) oxine ($T^{1}/2$ = 67.92 h) for cell labeling; indium (In-111) DTPA for cisternography ($T^{1}/2$ = 67.92 h).

Suggestions from the medical community for additional cyclotron-produced needs are welcome.

Inquiries concerning the availability, price schedule, and technical information on specific radiopharmaceuticals should be directed to: Abbass H. Al-Marzouky, MD, Executive Director, Research Centre, King Faisal Specialist Hospital and Research Centre, P.O. Box 3354, Riyadh 11211, Saudi Arabia (Fax No. 966-1-441-4839).

Joint Board for Postgraduate Medical Education Symposia for 1411

The Joint Board for Postgraduate Education is pleased to announce the following symposia for 1411.

1. 6th Annual Paediatric Symposium, College of Medicine and King Khalid University Hospital, 26-27 Rajab 1411 (10-11 February 1991).
2. 4th Saudi Gastroenterology and Hepatology Symposium; Security Forces Hospital, 10-12 Shaban 1411 (24-26 February 1991).
3. Advances in Thrombosis Management Symposium; Riyadh Central Hospital, 17-18 Shaban 1411 (3-4 March 1991).
4. Postgraduate and Continuing Medical Education; College of Medicine, King Saud University, 21-22 Shawwal 1411 (5-6 May 1991).

For further information, contact the Joint Board Office, College of Medicine, King Saud University, P.O. Box 2925, Riyadh 11461, Saudi Arabia; telephone (01) 467-1556 or 1564; telefax 481-1853; telex 403748 DARAYAH SJ.

King Faisal Specialist Hospital and Research Centre Symposia for 1411

King Faisal Specialist Hospital and Research Centre is pleased to announce the following educational activities for 1411.

1. Symposium on Therapy of Parasitic Diseases:

Advances and Problems; 28–29 Rajab 1411 (12–13 February 1991)
2. Molecular Biology of Cancer Symposium; 11–13 Shaban 1411 (25–27 February 1991)
3. FMGEMS Examination; 12–13 Muharram 1412 (23–24 July 1991)

For further information, contact Academic Affairs and Postgraduate Education, King Faisal Specialist Hospital and Research Centre, P.O. Box 3354, Riyadh 11211; telephone 464-7272, extension 1865 or 1834, fax 442-7237.

*Sponsored by the Joint Board for Postgraduate Medical Education.

Meeting of the Saudi Heart Association

The fourth scientific session of the Saudi Heart Association will be held in Riyadh from 12 to 14 February 1991. There will be original works relating to all aspects of cardiovascular diseases with particular emphases on coronary artery vascular disease, valvular heart disease, pericardial disease, interventional cardiology, noninvasive cardiology, infective endocarditis, cardiac surgery, pediatric cardiology, and cardiac anesthesia. Further information regarding the meeting may be obtained from the Saudi Heart Association, King Saud University, P.O.Box 2925, Riyadh 11461; tel: 467-1556 or 467-1551.

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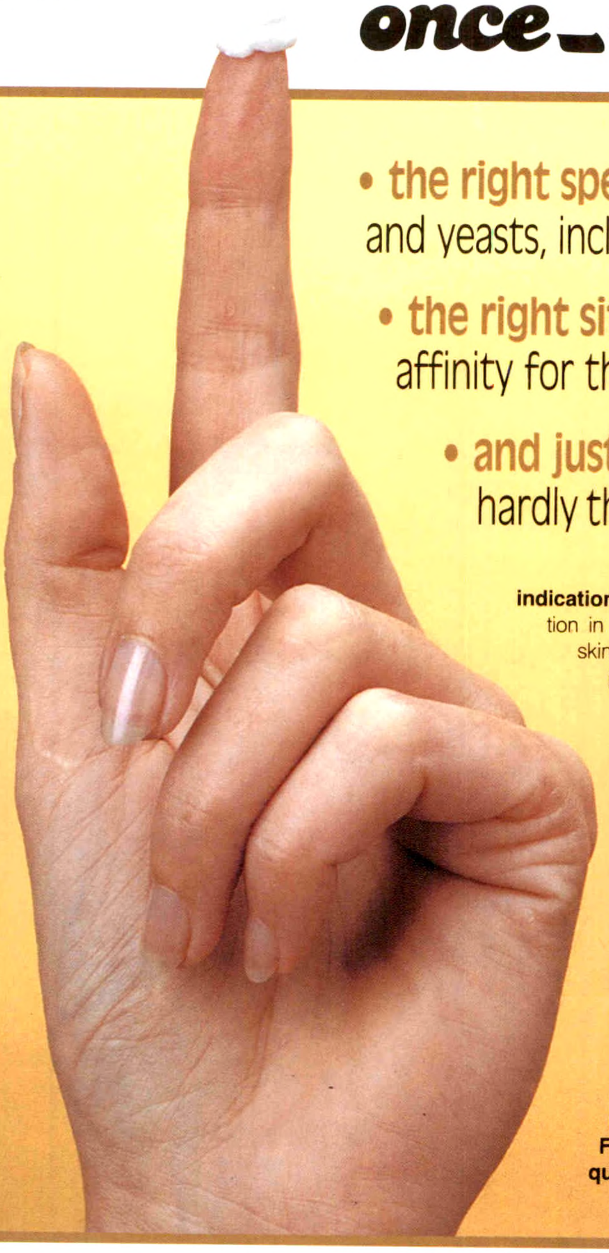

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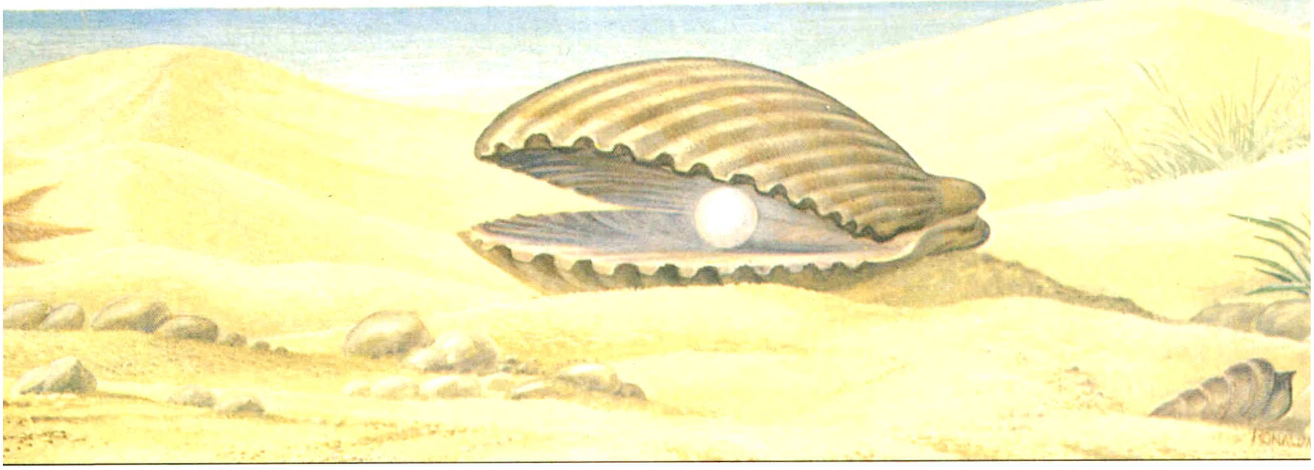

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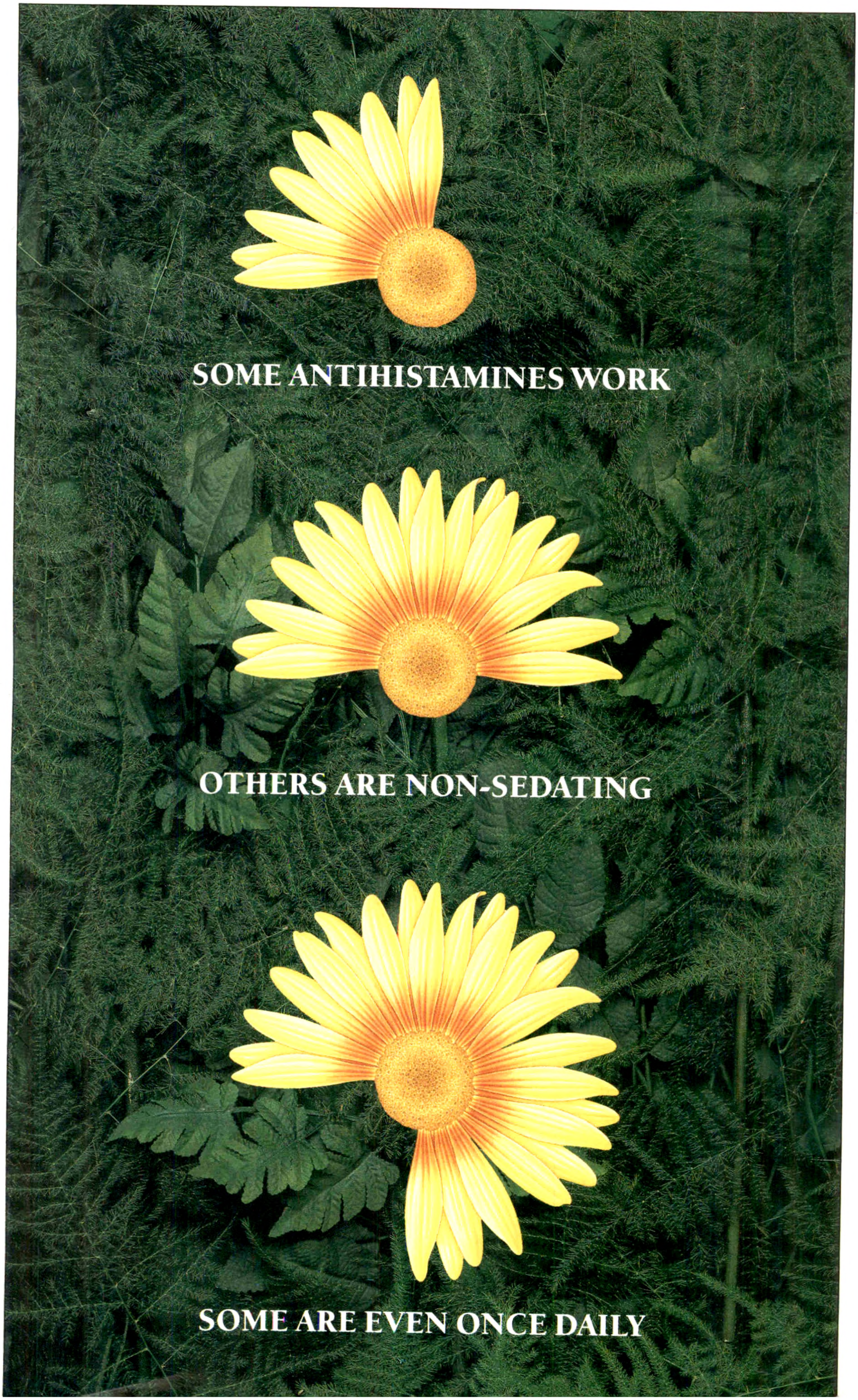
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فرجينيا جي كروزير
شيرلي موفيت

المدونات الطبية السعودية مجلة تنشر بموجب الأمر الملكي السامي رقم ٥/م/٢٤٢٢٣ بتاريخ ١٤ شوال عام ١٤٠٠هـ. وتصدر مرة كل شهرين، وهي مشروع مشترك بين كل من كلية الطب ومستشفى الملك خالد الجامعي ـ جامعة الملك سعود، صندوق بريد ٢٩٢٥ ـ الرياض ١١٤٦١، المملكة العربية السعودية، ومستشفى الملك فيصل التخصصي ومركز الأبحاث، صندوق بريد ٣٣٥٤ ـ الرياض ١١٢١١، المملكة العربية السعودية. يتم صف وطبع المجلة بمطابع جامعة الملك سعود. يتم توزيع المدوَّنات بواسطة قسم البريد التابع لإدارة الخدمات الإدارية بمستشفى الملك فيصل التخصصي ومركز الأبحاث. كما يتولى قسم الترجمة في هذه الإدارة إعداد الملخصات العربية بالاشتراك مع الدكتور محمد زهير القاوي. كل المراسلات والاستفسارات وطرق الحصول على المستلات ترسل إلى مكتب المطبوعات على العنوان التالي:

مكتب المطبوعات
مدونات الطب السعودي
مستشفى الملك فيصل التخصصي ومركز الأبحاث
ص. ب ٣٣٥٤
الرياض ١١٢١١ ـ المملكة العربية السعودية

منـدوب الاعلانـات
بي آر سي المتحدة
ابسوم ـ سري ـ المملكة المتحدة

الآراء التي ترد في المقالات المنشورة تعبر عن رأي أصحابها فقط ولا تعبر عن وجهة نظر مجلة المدونات الطبية السعودية. لا يسمح بإعادة طبع أي جزء من المجلة أو نسخه بأي شكل وبأي وسيلة سواء أكانت إليكترونية أو آلية، بما في ذلك التصوير والتسجيل أو الإدخال في أي نظام حفظ أو استعادة معلومات إليكتروني، بدون الحصول على موافقة مسبقة من إدارة المجلة.

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The *Annals of Saudi Medicine* is published bimonthly and is a joint project of the King Saud University College of Medicine and King Khalid University Hospital, P.O. Box 2925, Riyadh 11461, Saudi Arabia, and King Faisal Specialist Hospital and Research Centre, P.O. Box 3354, Riyadh 11211, Saudi Arabia. It is typeset and printed at the King Saud University Press. The *Annals* is distributed and Arabic abstracts are prepared, in association with Dr. Zuheir Al-Kawi, by staff of the Office Services Department of the King Faisal Specialist Hospital and Research Centre. All correspondence, reprint, and subscription information requests should be addressed to the Publications Office. Subscription price SR25 per issue.

Publications Office
Annals of Saudi Medicine
King Faisal Specialist Hospital and Research Centre
P.O. Box 3354
Riyadh 11211, Saudi Arabia

Advertising Representative:
PRC Associates
St. Andrews House, 22-28 High Street
Epsom, Surrey KT19 8AH, UK
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Indexed by Current Contents, Excerpta Medica,
and Current Awareness in Biological Sciences.
ISSN 0256–4947

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ANNALS OF SAUDI MEDICINE

Aims and Scope

The *Annals of Saudi Medicine* is a joint project of the King Faisal Specialist Hospital and Research Centre and the King Saud University College of Medicine and King Khalid University Hospital. The journal is typeset and printed at the King Saud University Press, Riyadh, Saudi Arabia. Since July 1985, the *Annals* has incorporated *The King Faisal Specialist Hospital Medical Journal*, established in 1980.

The *Annals* is a bimonthly multidisciplinary medical journal. High-quality papers, written in English, dealing with aspects of clinical, academic or investigative medicine or research will be welcome. Emphasis is placed on matters relating to medicine in Saudi Arabia in particular, and the Middle East in general, though articles are welcome from anywhere in the world, and the *Annals* has worldwide readership.

The *Annals* publishes original articles, case reports, letters to the editor, editorials, and from time to time, special communications, commentaries, and review articles. Abstracts of meetings and symposia sponsored by the Joint Board for Postgraduate Medical Education of Saudi Arabia are published, and the proceedings of such symposia may be published if the Editorial Board considers them appropriate and relevant. The Editorial Board wishes to minimize delay between manuscript submission, decision, and publication, and accordingly authors are requested to follow carefully the instructions set out under "Information for Authors."

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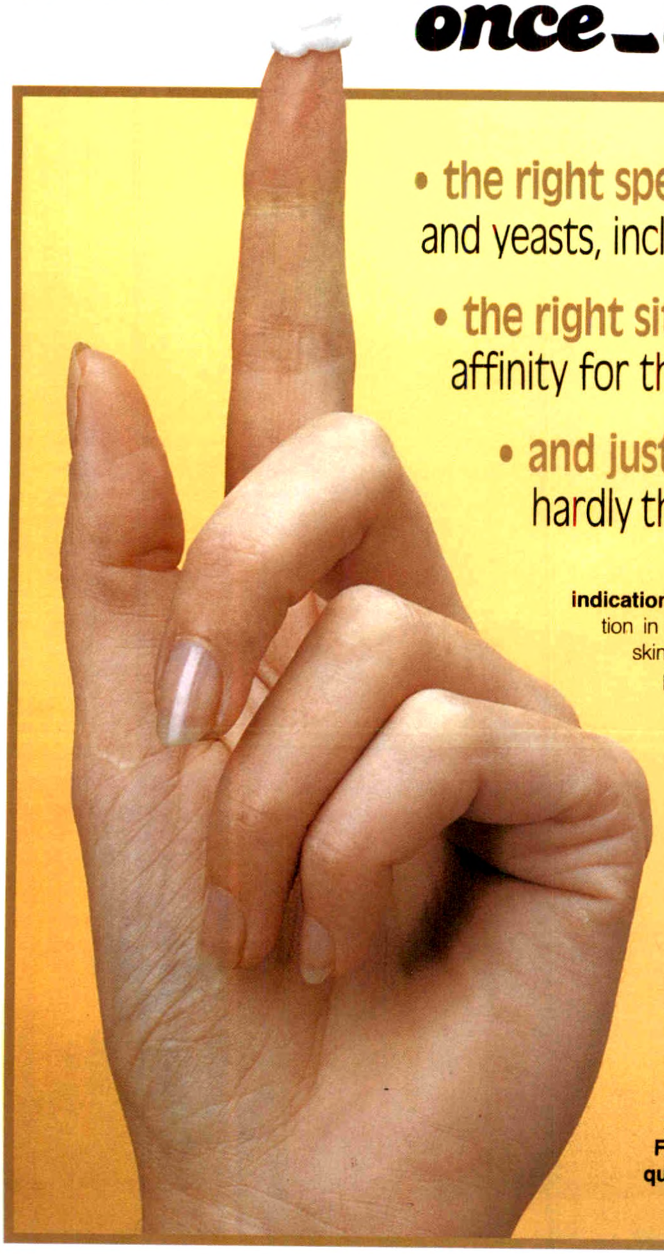

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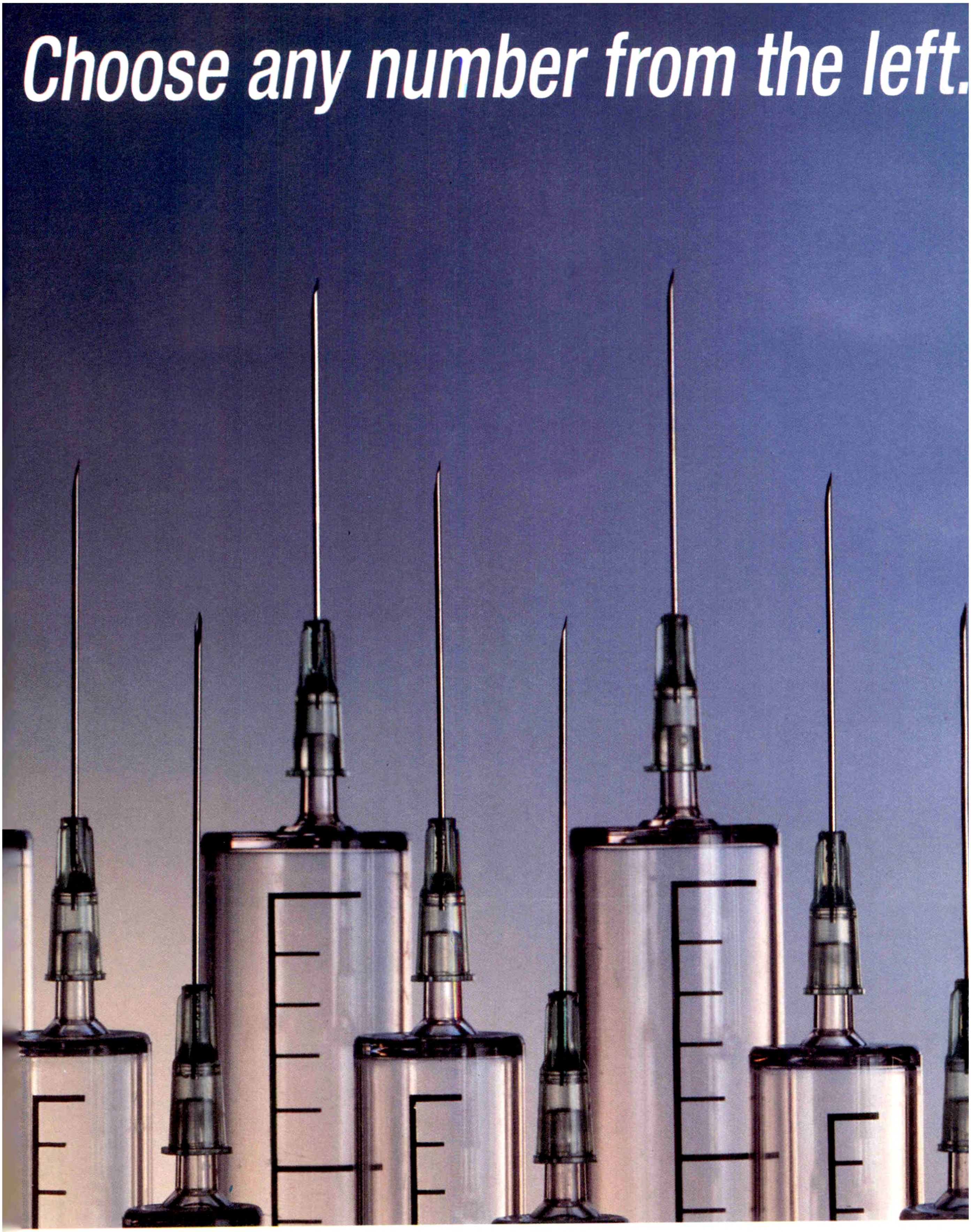

AUGMENTIN clavulanate-potentiated amoxycillin. **INDICATIONS. Upper Respiratory Tract Infections** e.g. Sinusitis, tonsillitis, otitis media. **Lower Respiratory Tract Infections** e.g. Acute and
bronchitis, lobar and bronchopneumonia, empyema, lung abscess. **Skin And Soft Tissue Infections** e.g. Boils/abscesses, cellulitis, wound infections, intra-abdominal sepsis. **Genito-Urina**
Infections e.g. Cystitis, urethritis, pyelonephritis, septic abortion, puerperal sepsis, pelvic infections, chancroid, gonorrhoea. **Other Infections** e.g. Osteomyelitis, septicaemia, peritonitis, post-o
infections. AUGMENTIN intravenous is also indicated for prophylaxis against infections which may be associated with major surgical procedures involving gastro-intestinal, pelvic, head and neck,
renal, biliary tract and joint replacement surgery. **DOSAGE. Adults and Children over 12 years** IV injection/infusion – Usually 1.2g 8 hourly. In more serious infections increase frequency to
intervals. **Children** IV Injection/Infusion – Children 3 months-12 years: Usually 30mg/kg* AUGMENTIN infusion 8 hourly. In more serious infections, increase frequency to 6 hourly intervals. Chil
months: 30mg/kg* AUGMENTIN every 12 hours in premature infants and in full term infants during the perinatal period, increasing to 8 hourly intervals thereafter. *Each 30mg AUGMENTIN intra
contains 25mg amoxycillin and 5mg clavulanic acid. Treatment with AUGMENTIN should not be extended beyond 14 days without review. **CONTRA-INDICATION.** Penicillin hypersensitivity. **PRECAU**
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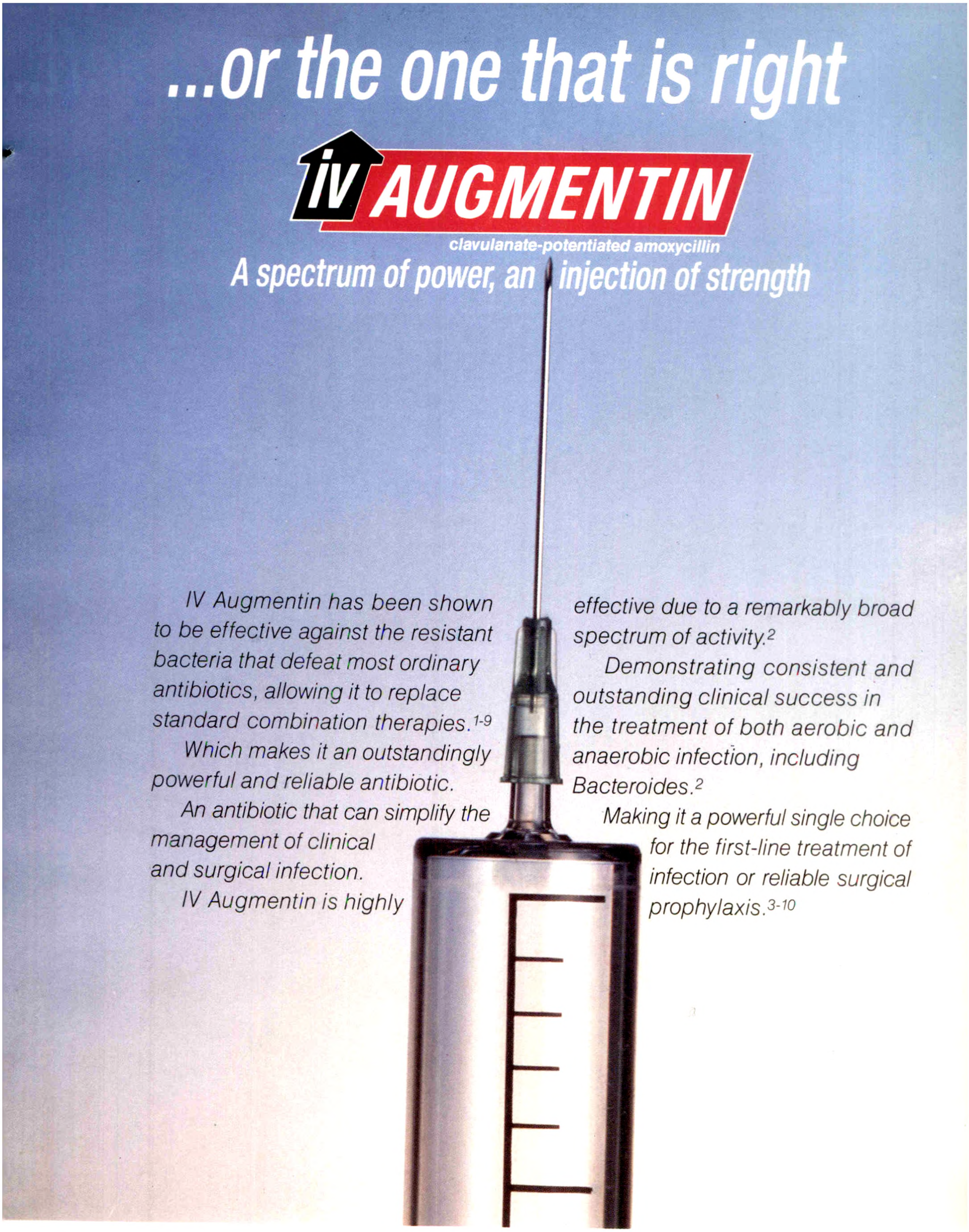
USE IN PREGNANCY AND LACTATION. Use of AUGMENTIN in pregnancy is not recommended unless considered essential by the physician. During lactation, trace quantities of penicillins
detected in breast milk. **SIDE-EFFECTS.** Side-effects, as with amoxycillin, are uncommon and mainly of a mild and transitory nature. Diarrhoea, pseudomembranous colitis, indigestion, nausea,



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candidiasis have been reported. Phlebitis at the site of injection has also been reported. Urticarial and erythematous rashes sometimes occur but their incidence has been particularly low in clinical
ls. An urticarial rash suggests penicillin hypersensitivity and treatment should be discontinued. Erythematous rashes are frequently mild and transient but may be severe when associated with infectious
nonucleosis, in which case treatment should be discontinued. Rare cases of erythema multiforme, Stevens-Johnson syndrome and an occasional case of exfoliative dermatitis have been reported.
ious and occasionally fatal hypersensitivity (anaphylactic) reactions and angioneurotic oedema have been reported in patients on penicillin therapy. These reactions are more likely to occur in individuals
a history of penicillin hypersensitivity and/or a history of sensitivity to multiple allergens. Hepatitis and cholestatic jaundice have been reported. ***AVAILABILITY.*** *600mg AUGMENTIN intravenous vials:*
ch containing 500mg amoxycillin and 100mg clavulanic acid. 1.2g AUGMENTIN intravenous vials. Each containing 1g amoxycillin and 200mg clavulanic acid. In IV presentations amoxycillin is present
the sodium salt and clavulanic acid is present as the potassium salt. Each 1.2g vial contains approximately 1.0 mmol of potassium and 3.1 mmol of sodium. Not all presentations are available in every
ntry. Further information is available on request from SmithKline Beecham Pharmaceuticals International, Brentford, England. AUGMENTIN is a product of research from
echam Pharmaceuticals International, Brentford, England. Augmentin is a trade mark. **REFERENCES:** 1. Green-Thompson RW et al. *Proc 13th ICC Vienna* 1983; **(79):** 17
Abbas AMA et al. *Excerpta Medica* 1980; **ICS 544:** 173. 3. Tehan S, Whittaker J. *Surg Res Commun* 1989; **6:** 97. 4. Levi D et al. *Pharmatherapeutica* 1989; **5:** 355
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IMPORTANT NOTICE The World Health Organisation (WHO*) has recommended that pregnant women and new mothers be informed of the benefits and superiority of breastfeeding – in particular the fact that it provides the best nutrition and protection from illness for babies.

Mothers should be given guidance on the preparation for, and maintenance of, lactation, with special emphasis on the importance of a well-balanced diet both during pregnancy and after delivery. Unnecessary introduction of partial bottle-feeding or other foods and drinks should be discouraged since it will have a negative effect on breastfeeding. Similarly, mothers should be warned of the difficulty of reversing a decision not to breast-feed.

Before advising a mother to use an infant formula, she should be advised of the social and financial implications of her decision: for example, if a baby is exclusively bottle-fed, more than one can (450 g) per week will be needed, so the family circumstances and costs should be kept in mind. Mothers should be reminded that breast-milk is not only the best, but also the most economical food for babies.

If a decision to use an infant formula is taken, it is important to give instruction on correct preparation methods, emphasizing that unboiled water, unboiled bottles or incorrect dilution can all lead to illness.

* See: International Code of Marketing of Breast Milk Substitutes, adopted by the World Health Assembly in Resolution WHA 34.22, May 1981.

Information for the medical profession only.

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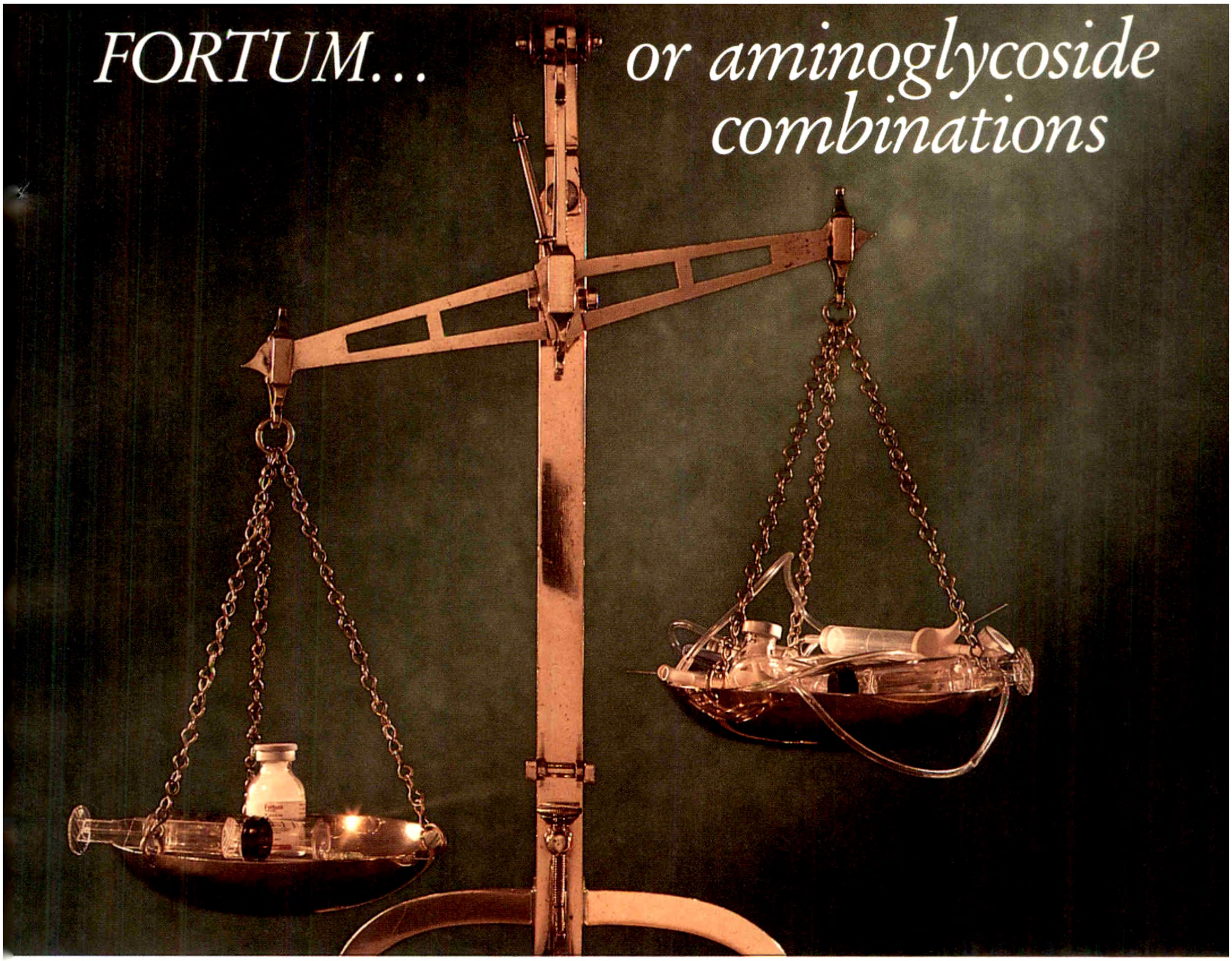

The choice is simple

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Fortum is a simple and effective approach to hospital acquired infections.

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Abbreviated Prescribing Information

Presentation: Fortum for injection is supplied in vials containing 250 mg, 500 mg, 1 g and 2 g ceftazidime (as pentahydrate) with sodium carbonate. **Uses:** Fortum is a bactericidal cephalosporin antibiotic which is resistant to most beta-lactamases and is active against a wide range of Gram-positive and Gram-negative bacteria. It is indicated for the treatment of single infections and for mixed infections caused by two or more susceptible organisms. Fortum, because of its broad antibacterial spectrum, may be used alone as first choice drug, pending sensitivity test results. **Dosage and administration:** Adults: 1 g to 6 g i.m. or i.v. per day and by the i.p. route 125 to 250 mg per two litres of dialysis fluid (see Data Sheet for details). Neonates, Infants and Children: Up to two months: 25 to 60 mg/kg/day given as two divided doses has proved to be effective. In the neonate the serum half-life of ceftazidime can be three to four times that in adults. Over two months: 30 to 100 mg/kg/day given as two or three divided doses (see Data Sheet for details). In Impaired Renal Function: the dosage of ceftazidime should be reduced when the glomerular filtration rate (GFR) falls below 50 ml/min. An initial loading dose of 1 g may be given to patients with suspected renal insufficiency (See Data Sheet for details). **Contra-indication:** Fortum is contra-indicated in patients with known hypersensitivity to cephalosporin antibiotics.
Precautions: Cephalosporins may, in general, be given safely to patients who are hypersensitive to penicillins. Care is indicated in patients who have experienced an anaphylactic reaction to penicillin. Cephalosporin antibiotics at high dosage should be given with caution to patients receiving concurrent treatment with nephrotoxic drugs. Clinical experience with Fortum has shown that this is not likely to be a problem at the recommended dose levels. As with all drugs, Fortum should be administered with caution during the early months of pregnancy and in early infancy. Fortum is excreted in human milk in low concentrations. Fortum does not interfere with enzyme-based tests for glycosuria. Slight interference with copper reduction methods may be observed. Fortum does not interfere in the alkaline picrate assay for creatinine. Fortum and aminoglycosides should not be mixed in the same giving set or syringe. As with other broad spectrum antibiotics, prolonged use of Fortum may result in the overgrowth of non-susceptible organisms (e.g., Candida, Enterococci) which may require interruption of treatment or adoption of appropriate measures. **Side effects:** Fortum is generally well tolerated with only infrequent adverse reactions, e.g. pain and/or inflammation after i.m. administration and phlebitis and/or thrombophlebitis after i.v. administration, rashes, fever, pruritus, anaphylaxis, gastrointestinal disturbances, headache, dizziness, paraesthesia and bad taste. Transient changes in laboratory values may occur including: eosinophilia, a positive Coombs' test, thrombocytosis, leucopenia, thrombocytopenia and slight rises in hepatic enzymes.

Glaxo For full prescribing information see data sheet or contact: **Glaxomed Limited**, International House,
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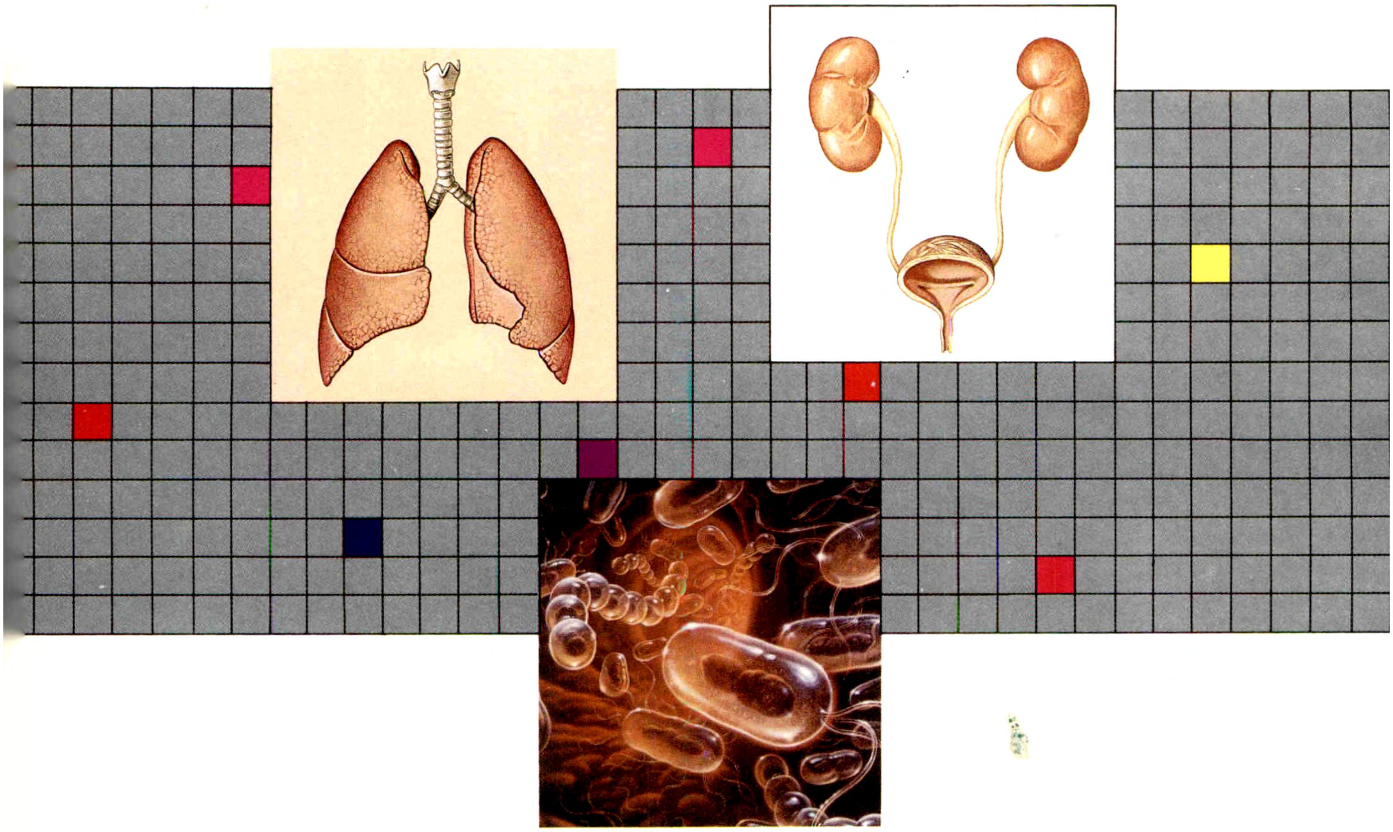

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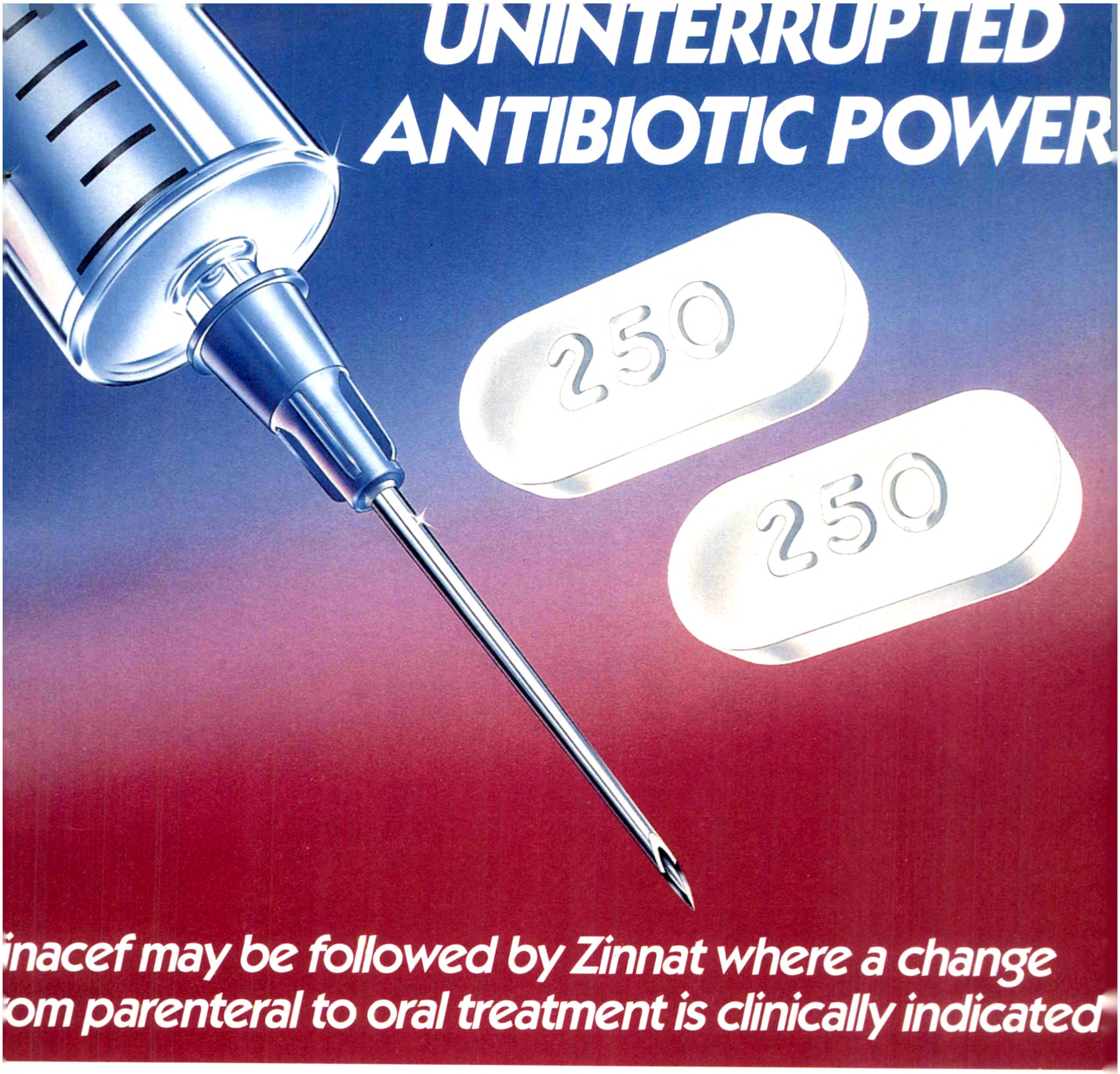
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R DECISIVE PARENTERAL EFFECT

EF ABBREVIATED PRESCRIBING INFORMATION

Adults: Generally 750mg t.i.d.i.m. or i.v. Severe infections 1.5g t.i.d.i.v. Frequency of injections can be increased
ly if necessary. *Infants and children:* 30 to 100mg/kg/day in 3 or 4 divided doses. 60mg/kg/day will be appropriate
nfections. *Neonates:* 30 to 100mg/kg/day in 2 or 3 divided doses. *Gonorrhoea:* Single dose of 1.5g (2 x 750mg into
sites). *Prophylaxis:* The usual dose of 1.5g i.v. with induction of anaesthesia for abdominal, pelvic and orthopaedic
s, may be supplemented with two 750mg i.m. doses 8 and 16 hours later. In cardiac, pulmonary, oesophageal and
operations, the usual dose is 1.5g i.v. with induction of anaesthesia continuing with 750mg i.m. t.i.d. for a further
ours. In total joint replacement, 1.5g cefuroxime powder may be mixed dry with each pack of methyl methacrylate
polymer before adding the liquid monomer. **Contra-indication:** Hypersensitivity to cephalosporins.
ns: Cephalosporins may, in general, be given safely to patients who are hypersensitive to penicillins. Care is
in patients who have experienced an anaphylactic reaction to penicillin. As with all drugs, Zinacef should be
red with caution during the early months of pregnancy. Zinacef should not be mixed in the syringe with
coside antibiotics. Reduce dosage when renal function is markedly impaired. (See data sheet for details.)
porins at high dosage should be given with caution to patients receiving concurrent treatment with potent diuretics
rusemide, as these combinations are suspected of adversely affecting renal function. Clinical experience with
s shown that this is not likely to be a problem at the recommended dose levels. **Side effects:** Adverse reactions are
generally mild and transient, e.g., hypersensitivity reactions (rashes and rarely anaphylaxis), gastro-intestinal
ces, decreased haemoglobin concentration, eosinophilia, leucopenia, neutropenia and a positive Coombs' test.
rises in serum liver enzymes. Transient pain after i.m. injection. As with other antibiotics, prolonged use may result
rgrowth of non-susceptible organisms, e.g. Candida. **Package quantities:** Zinacef 250mg or Zinacef 750mg (for
ramuscular or intravenous injection) in packs of 5. Zinacef 1.5g (for use by intravenous injection), packed singly.
5g infusion packs (for use by intravenous infusion), packed singly.

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ZINNAT

cefuroxime axetil

FOR RELIABLE ORAL POWE

ZINNAT ABBREVIATED PRESCRIBING INFORMATION

Uses ZINNAT is indicated for infections of lower respiratory tract, ear, nose and throat, urinary tract, skin and soft tissu
Presentation White tablets containing 125mg, 250mg and 500mg cefuroxime as cefuroxime axetil. **Dosage** *Adults:* Mo
infections – 250mg twice daily. Lower respiratory tract infection – 250mg twice daily, Pneumonia – 500mg twice dail
Urinary tract infection – 125mg twice daily, Pyelonephritis – 250mg twice daily. Uncomplicated gonorrhoea – 1g sing
dose. *Children:* Most infections – 125mg twice daily. Otitis media – 250mg twice daily. Tablets should not be chewed
crushed and therefore are not suitable for children under five years of age. ZINNAT should be taken after food for optimu
absorption. **Contra-indications** Hypersensitivity to cephalosporin antibiotics. **Precautions** ZINNAT may in general be giv
safely to patients who are hypersensitive to penicillins, although cross-reactions have been reported with so
cephalosporins and special care is indicated in patients who have experienced anaphylactic reaction to penicillin
Cefuroxime axetil should be administered with caution during early months of pregnancy. **Side effects** Gastrointesti
disturbances including diarrhoea, nausea and vomiting have been reported, these are generally mild and transient in natur
As with all broad spectrum antibiotics, there have been rare reports of pseudomembranous colitis. Rarely, hypersensitiv
reactions, eosinophilia, and transient increases of hepatic enzyme levels have been noted. **Package quantities** All strengths
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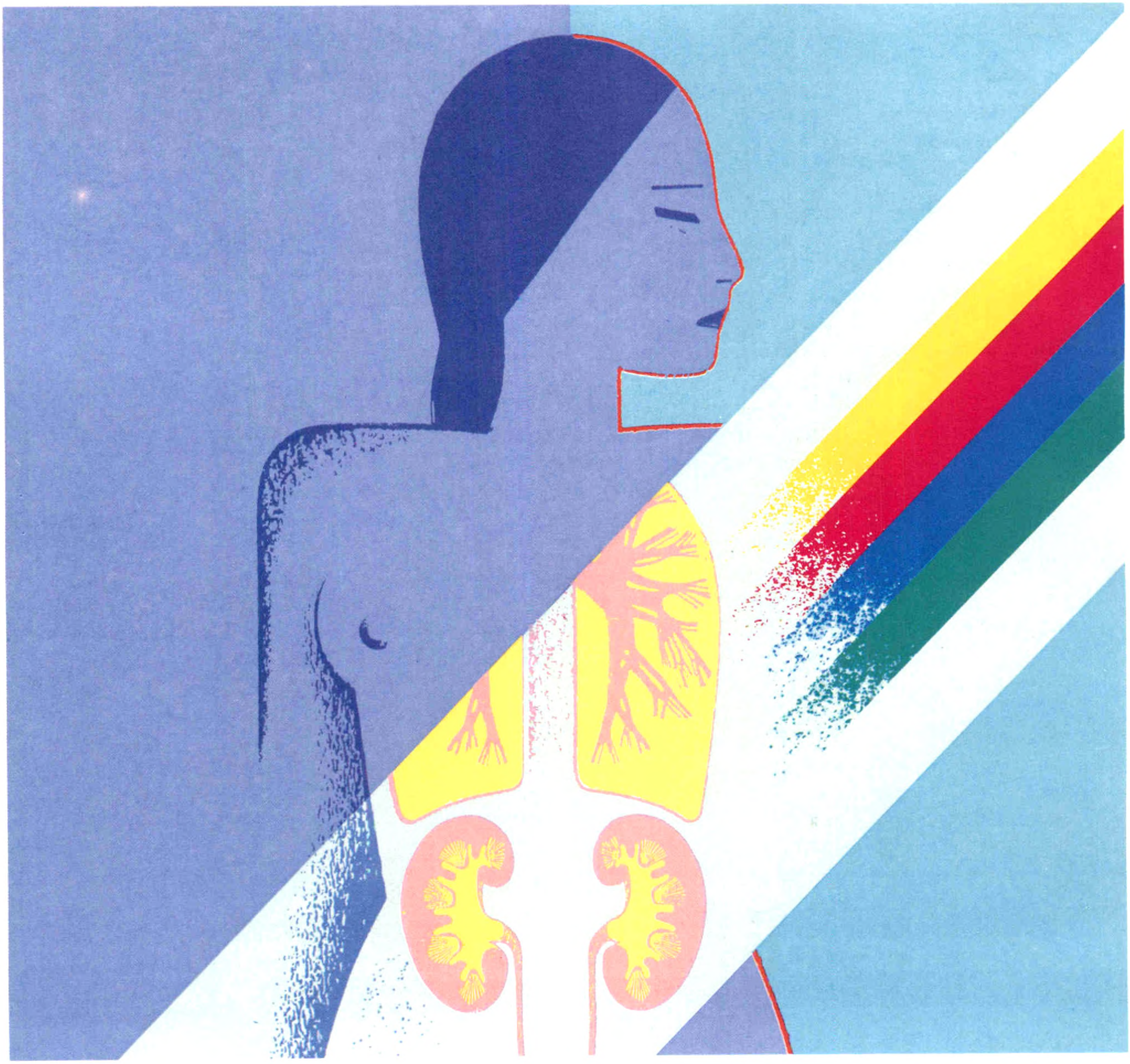

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Editorial

TOBACCO AND THE THIRD WORLD

The association of cigarette smoking with coronary artery disease, chronic bronchitis, carcinoma of the bronchus, peptic ulcer, and cancer of the tongue, larynx, esophagus, and urinary bladder is well known [1]. The annual toll of premature deaths attributable to tobacco use will be approximately three million worldwide in the 1990s, and this will rise to ten million by the year 2025 [2]. While cigarette consumption is decreasing in the industrialized world by about 1% a year, in Asia and Latin America, it is exceeding the population growth by 7%, and in Africa by 18% [3].

In this issue of the *Annals*, there are three tobacco-use–related papers; two on cigarette-smoking habits in Riyadh and Amman [4,5] and the third on jurak smoking [6]. Taha et al [4] report on the smoking habits of 2264 male students at King Saud University in Riyadh. They found that 37% of the students smoke and over half smoke more than 15 cigarettes per day. Thirty-six percent started smoking between the ages of 10 and 15 years. The authors recommend that an antismoking campaign should be mounted in the schools and that the Saudi government should consider legislation to prohibit the sale of tobacco to anyone younger than 18 years old.

The second study comes from Jordan where Awidi [5] studied the pattern of smoking in greater Amman among 3489 individuals from various socioeconomic classes. The results indicated that 58.8% of the males and 27.4% of the females in the nonstudent population were smokers, compared with 30.8% of the males and 7.4% of the females in the student population. Smoking was more common among illiterate individuals (71.4%) than among individuals with various levels of education (range, 43.2 to 55.6%). Smoking was also more common among skilled and nonskilled workers than among professionals (58.1% versus 43.6%). Both Taha and Awidi's study revealed a high smoking prevalence among students and the general population in Riyadh and Amman. The findings in these studies are alarming and indicate that, unless an active antismoking campaign is mounted, epidemics of smoking-related diseases may occur in the near future.

The third study comes from Jeddah where Khoja et al [6] studied the effect of jurak smoke condensate on the activities of four enzymes in the mouse liver and intestine. The levels of these enzymes were significantly affected, indicating that the substance is toxic. The authors concluded that the low content of tobacco leaves in jurak paste and filtration of the smoke by water in the sheesha reservoir are not sufficient to make the smoke risk free.

In a recent study [7] on the smoking habits of 698 physicians in Riyadh, it was found that 38% of the male physicians and 16% of the female physicians are smokers and that 80% do not smoke at work. In the United States, 8% of the physicians and dentists smoke [8,9]. It is therefore obvious that smoking is much more common in this part of the world compared with that observed for industrialized countries, and this appears to be true for most Third World countries. The arguments used in the West to discourage smoking must be adopted to make them more relevant to Third World countries. Four arguments recommended by the International Union against Cancer [10] include: diseases caused by smoking place an additional burden on the health care system when infectious diseases and malnutrition still must be dealt with; buying cigarettes when there is dire poverty uses money needed for food; tobacco curing results in deforestation, which has a serious impact on the environment; and most developing countries have a large deficit balance of trade in tobacco, importing far more than they either produce or export. Third World countries must work on prevention and antismoking campaigns, as they translate into cost-effective measures that the country at large can benefit from.

Worldwide, little money and effort are spent to combat cigarette smoking. In 1990 the United States spent $3.8 million on antitobacco activities compared with $2.6 billion spent annually by the tobacco industry for advertising and promotion [11]. It is ironic that tobacco, which is both toxic and lethal and is responsible for millions of deaths around the world, is ignored by health planners and decision makers. Antismoking campaigns must receive more attention if lives are to be saved.

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Original Articles

EFFECTS OF JURAK SMOKE CONDENSATE ON ENZYME ACTIVITY OF THE MOUSE

Samir M. Khoja, MMedSci, DPhil; Mahmoud M. El-Merzabani, PhD;
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استقصى أثر مكثّف دخان الجراك على نشاطات انظيهات الفسفاتاز القلوية وغلوكوز ـ ٦ فسفاتاز ونوكليوتيداز ـ ٥ وكولينيستيراز للأمعاء الدقيقة والكبد لدى الفئران. زودت الفئران بمكثّف الدخان عبر أنبوب من الفم إلى المعدة بمعدل خمس مرات في الأسبوع ولمدة ثلاث أشهر. استخدم خمسة عشر حيواناً في الشهر الأول والثاني والثالث بعد إعطاء الجراك وتم قتل خمسة فئران في الشهر الأول والخامس والتاسع ثم نزع منها الكبد والأمعاء الدقيقة لمقايسة الأنظيهات. كانت نشاطات الأنظيهات الأربعة، المعروفة بحساسيتها للعوامل السامة، متأثرة تأثيراً ملموساً. تشير هذه النتائج إلى أن تدني نسبة التبغ في معجونة الجراك وترشيح الدخان بواسطة الماء الموجود في إناء الشيشة لا يكفيان لجعل الدخان الذي يستنشقه المدخنون خاليا من المخاطر.

The effect of jurak smoke condensate on the activities of alkaline phosphatase, glucose 6-phosphatase, 5'-nucleotidase, and cholinesterase of mouse liver and small intestine was investigated. Jurak smoke condensate was administered orally by stomach tube five times weekly over a three-month period. Fifteen animals were used at 1, 2, and 3 months after the start of the administration, with 5 animals killed on days 1, 5, and 9, and the liver and small intestine removed for enzyme assays. The activities of all four enzymes, which are known to be sensitive to toxic agents, were significantly affected. These results indicate that the low content of tobacco leaves in jurak paste and the filtration of the smoke by water in the sheesha reservoir are not sufficient to make the smoke inhaled by smokers risk free.

Cigarette smoking is common among both males and females throughout the world, and has been implicated in a variety of diseases. Smoking increases the risk of lung cancer, heart disease, and respiratory diseases of all kinds [1].

Jurak (a mixture of tobacco and fruits cooked to produce a dark paste) is popular as the ingredient for hubble-bubbles (sheesha). Although many Saudi subjects of both sexes and various ages are regular sheesha smokers, little experimental and clinical research has been done on the effects of sheesha smoking. It is generally believed by sheesha smokers, however, that jurak smoking is not as dangerous as cigarette smoking because there is no tobacco in the mixture.

The chemical composition of jurak smoke condensate has been analyzed [2], and of 142 chemical compounds detected, only 88 were found in the smoke condensate. These include alkenes and alkynes; alkaloids and other bases; and alcohols, aldehydes, and ketones. The polynuclear aromatic hydrocarbons—the major carcinogenic agents in cigarette smoke—were not detected in jurak smoke condensate. However, El-Aaser et al [3] discovered 16 metals in jurak paste and jurak smoke condensate. It has also been found that, of 14.7 mg of metals contained in 1 gm of jurak paste, only 3.1 μg was transferred to the inhalant smoke. This indicates that the water in the sheesha reservoir does retain some of the organic and metallic inhalants by acting as a solvent and a condensation medium, and thus the carcinogenic effect of the metallic compounds in jurak smoke is reduced.

In an assessment of the risk factors prevalent among Saudi citizens for smoking-related diseases, serum levels of carboxyhemoglobin among

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Accepted for publication 17 April 1990.

jurak smokers were found to be significantly higher than those in cigarette smokers and nonsmokers [4,5]. Zahran et al [4,5,] attributed this finding to the carbon monoxide produced from jurak and charcoal. In another study of the effect of sheesha smoke on animal models, the carboxyhemoglobin levels of sheesha-exposed rats were found to be significantly higher than those in normal control rats [6].

We evaluated the long-term oral administration of jurak smoke condensate and its effect on mouse liver and small intestine. The activities of alkaline phosphatase, 5'-nucleotidase, glucose-6-phosphatase, and cholinesterase were determined to monitor the initial damage, if any, and to follow up its rate of recovery. The liver was selected because it is the major site of xenobiotic metabolism, whereas the small intestine was selected because it represents a tissue with a high regeneration rate and is highly affected by cytotoxic agents.

Material and Methods

All biochemicals were obtained from Fluka Chemical Co, Switzerland, and used without further purification. All chemicals were analytical grade and were obtained from BDH, England.

Male albino mice (20–25 gm) were obtained from King Fahd Medical Research Center. They were fed a standard laboratory diet, ad libitum, with free access to water.

Preparation of Jurak Smoke Condensate

Jurak smoke condensate was prepared as previously described [2]. In this method, patches (100 gm each of jurak paste) were burned under conditions which simulated sheesha smoking. Smoke was drawn through a water reservoir and then through an ice-cooled chloroform trap. The contents of the trap were dehydrated with anhydrous sodium sulfate and the condensate was obtained after evaporating the chloroform at 45°C under reduced pressure.

Administration of Jurak Smoke Condensate

Jurak smoke condensate obtained from the previous step was emulsified in Tween-80, after the evaporation of chloroform, and diluted with a physiological saline so that each milliliter was equivalent to 1 gm of jurak paste. The emulsion was distributed in small dark brown bottles (15 ml) and stored at 4°C until use. Forty-five mice were used in the experimental group, in which 0.2 ml of condensate was administered orally by a stomach tube five times weekly for three months. The dose was estimated to be 8 to 10 gm/kg of body weight which is about four to five times the amount smoked daily by the average smoker. The relatively high dose was used to overcome the difficulty encountered in absorption from the intestine as compared with the lung, which is the normal route of smoking. A control group of 15 animals received 0.2 ml of saline diluted with Tween-80.

Preparation of Tissue Homogenates

Every 30 days after the first administration, 15 animals from the experimental group were withdrawn. Five experimental animals and five control animals were killed by cervical dislocation. The remaining ten animals were maintained on a normal diet without any treatment and a group of five each were killed on days 5 and 9 after the last injection. The liver and the jejunum of each animal were quickly removed, washed, and flushed with ice-cold saline solution. Tissues were then blotted dry on filter paper and homogenized with 10 volumes (w/v) of ice-cold bi-distilled water using a Potter Elvehjem glass homogenizer fitted with a Teflon pestle. The homogenates were stored at –20°C until use, except for glucose 6-phosphatase which was assayed in the fresh homogenate.

Enzymes Assays

The activity of glucose-6-phosphatase was measured at pH 6.5 at 37°C according to the method of Swanson [7]. One unit of activity was defined as the formation of 1 μmol of inorganic phosphate/min.

5'-Nucleotidase activity was measured at pH 7.5 at 37°C using 5'-adenosine monophosphate as a substrate following the method described by El-Aaser and El-Merzabani [8], and the liberated inorganic phosphate content was determined by the method of Fiske and Subbarow [9]. One unit of activity was defined as the formation of 1 μmol of inorganic phosphate/min.

Alkaline phosphatase activity was measured at pH 10.0 at 37°C according to the method of Fujita [10]. One unit of activity is defined as the formation of 1 μmol of *p*-nitrophenol/min.

Tissue cholinesterase activity was measured at pH 8 at 37°C according to the method of de la Huerga et al [11]. This method is based on the chemical determination of the unreacted substrate (acetylcholine bromide). One unit of activity corresponded to the hydrolysis of 1 μmol of acetylcholine/min.

Expression of Results

All maximal enzyme activities are expressed as μmol/min per gram of tissue wet weight. The results are expressed as means ± SD and comparisons between controls and experimental data were done using Student's *t* test.

Results

The one-month treatment of mice with jurak smoke condensate caused a significant increase in the activity of liver alkaline phosphatase ($P < 0.05$) with a sign of recovery on day 9, but the activity was still 77.4% higher than normal (Table 1). Intestinal alkaline phosphatase activity of the same age group showed a progressive increase that reached 99.8% on day 9. Conversely, animals treated for two or three months showed a significant decrease on day 1 ($P < 0.05$). Recovery to nearly normal levels was reached on day 5 in the liver and day 9 in the small intestine.

Liver 5'-nucleotidase activity was significantly increased ($P < 0.01$) in mice treated for one month, whereas the enzyme activity was significantly decreased in mice treated for two or three months ($P < 0.05$) (Table 2). In all three groups, 9 days were not sufficient to restore normal enzyme activity. In the small intestine, however, the three groups showed a significant decrease ($P < 0.01$) in the activity of 5'-nucleotidase, but 9 days again were not sufficient for the return of normal activity.

Liver glucose 6-phosphatase activities determined on day 1, after one, two, and three months of treatment, were significantly decreased ($P < 0.01$), and normal enzyme activity was reached on day 9 after the end of condensate treatment (Table 3). A similar pattern was also observed in the small intestine, although the enzyme activity on day 9 was still 38.1% lower ($P < 0.01$) than normal in animals treated for one month. However, animals treated for two and three months showed a nonsignificant difference from normals, with decreased enzyme activities of only 13.2 and 18.1%, respectively.

Cholinesterase activity of the liver and small intestine was not significantly affected after one month of treatment (Table 4). However, the activity was significantly decreased ($P < 0.01$) in both tissues of mice treated for two and three months, and 9 days were not sufficient for the return of normal enzyme activity, as the activity was still significantly lower than normal by about 30% in both tissues.

TABLE 1. *Effects of repeated administration of jurak smoke condensate on alkaline phosphatase activity.*

Administration period (mo)	Time of assay after sacrificing (da)	Liver (units/gm wet weight)	(%)	Intestine (units/gm wet weight)	(%)
Control		0.460 ± 0.085		21.960 ± 4.236	
1	1	0.863 ± 0.405	(187.6)[b]	27.167 ± 5.010	(123.8)[a]
	5	0.944 ± 0.217	(205.2)[c]	34.214 ± 6.97	(155.8)[c]
	9	0.816 ± 0.237	(177.4)[c]	43.886 ± 2.216	(199.8)[c]
2	1	0.349 ± 0.039	(75.9)[b]	14.848 ± 2.299	(67.6)[b]
	5	0.414 ± 0.129	(90.0)[a]	13.199 ± 2.115	(60.1)[c]
	9	0.417 ± 0.099	(90.6)[a]	19.420 ± 7.46	(88.4)[a]
3	1	0.289 ± 0.048	(62.8)[c]	16.533 ± 4.528	(75.3)[b]
	5	0.452 ± 0.013	(98.3)[a]	18.247 ± 5.784	(83.3)[a]
	9	0.418 ± 0.071	(90.8)[a]	20.444 ± 2.756	(93.1)[a]

Activity is expressed as μmole *p*–nitrophenol/min/gm weight, and values in parentheses are percentages, with untreated controls as 100%.

[a] Nonsignificant; [b] $P < 0.05$; [c] $P < 0.01$.

TABLE 2. *Effects of repeated administration of jurak smoke condensate on 5′-nucleotidase activity.*

Administration period (mo)	Time of assay after sacrificing (da)	Liver (units/gm wet weight)	(%)	Intestine (units/gm wet weight)	(%)
Control		1.910 ± 0.250		4.43 ± 0.258	
1	1	2.076 ± 0.826	(108.7)[a]	2.765 ± 0.784	(62.4)[c]
	5	3.080 ± 1.33	(161.3)[c]	4.546 ± 0.839	(102.6)[a]
	9	1.632 ± 0.382	(85.4)[a]	5.408 ± 0.538	(122.1)[b]
2	1	1.344 ± 0.587	(70.4)[b]	2.480 ± 0.301	(56.0)[c]
	5	1.304 ± 0.324	(63.3)[c]	2.425 ± 0.290	(54.7)[c]
	9	1.402 ± 0.133	(73.4)[c]	2.651 ± 0.300	(59.8)[c]
3	1	1.526 ± 0.093	(80.0)[a]	2.794 ± 0.354	(63.1)[c]
	5	1.853 ± 0.524	(97.0)[a]	2.895 ± 0.776	(65.3)[c]
	9	0.922 ± 0.412	(48.3)[c]	3.645 ± 0.463	(82.3)[c]

Activity is expressed as μmole P_i/min/gm wet weight, and values in parentheses are percentages, with untreated controls as 100%.
[a] Nonsignificant; [b] $P < 0.05$; [c] $P < 0.01$.

TABLE 3. *Effects of repeated administration of jurak smoke condensate on glucose 6-phosphatase activity.*

Administration period (mo)	Time of assay after sacrificing (da)	Liver (units/gm wet weight)	(%)	Intestine (units/gm wet weight)	(%)
	Control	12.576 ± 2.187		2.559 ± 0.293	
1	1	7.139 ± 0.972	(56.8)[c]	1.178 ± 0.097	(46.0)[c]
	5	8.621 ± 1.052	(68.6)[c]	1.330 ± 0.145	(52.0)[c]
	9	12.183 ± 1.558	(96.9)[a]	1.585 ± 0.241	(61.9)[c]
	Control	11.823 ± 1.400		2.401 ± 0.213	
2	1	6.144 ± 1.272	(52.0)[c]	1.136 ± 0.172	(47.3)[c]
	5	7.680 ± 0.852	(64.9)[c]	1.395 ± 0.231	(58.1)[c]
	9	10.894 ± 1.845	(92.1)[a]	2.084 ± 0.497	(86.8)[c]
	Control	12.074 ± 1.596		2.128 ± 0.133	
3	1	5.188 ± 1.034	(43.0)[c]	1.110 ± 0.140	(52.2)[c]
	5	6.370 ± 1.404	(52.8)[c]	1.244 ± 0.183	(58.4)[c]
	9	11.350 ± 1.314	(94.0)[a]	1.742 ± 0.453	(81.9)[a]

Activity is expressed as μmole P_i/min/gm wet weight, and values in parentheses are percentages, with untreated controls as 100%.
[a] Nonsignificant; [b] $P < 0.05$; [c] $P < 0.01$.

Discussion

Alkaline phosphatase and 5′-nucleotidase are membrane-bound enzymes and their serum levels are often used in the diagnosis of liver diseases and cellular damage. There is strong evidence that, when diseased, liver tissue forms excess amounts of these enzymes and releases them into the blood [12]. However, Jenkins et al [13] proved that determination of total enzyme activity in the liver is a more sensitive indicator of toxicity. In the present study, liver and intestinal alkaline phosphatase activities were significantly elevated after one month of treatment with the condensate, and 9 days were not sufficient for the return of normal enzyme levels. 5′-Nucleotidase activities in both the liver and small intestine were less sensitive to the effect of one month of treatment with the condensate. These results agree with data reported in rodents after short-term treatment with the hepa-

TABLE 4. *Effects of repeated administration of jurak smoke condensate on cholinesterase activity.*

Administration period (mo)	Time of assay after sacrificing (da)	Liver (units/gm wet weight)	(%)	Intestine (units/gm wet weight)	(%)
Control		4.178 ± 0.87		3.55 ± 0.17	
1	1	4.239 ± 1.00	(101.4)[a]	3.588 ± 1.33	(101.1)[a]
	5	4.878 ± 1.68	(116.0)[a]	4.083 ± 0.41	(115.0)[a]
	9	3.124 ± 0.54	(74.8)[b]	4.918 ± 0.93	(138.5)[a]
2	1	2.755 ± 0.36	(65.9)[c]	2.037 ± 0.39	(57.4)[c]
	5	2.981 ± 0.27	(71.4)[c]	2.131 ± 0.23	(60.0)[c]
	9	2.964 ± 0.40	(70.9)[c]	2.471 ± 0.67	(69.6)[c]
3	1	3.383 ± 0.39	(80.9)[b]	2.680 ± 0.39	(75.5)[c]
	5	3.339 ± 0.59	(79.9)[b]	2.276 ± 0.47	(64.1)[c]
	9	3.011 ± 0.35	(72.1)[c]	2.387 ± 0.28	(67.7)[c]

Activity is expressed as μmole choline/min/gm wet weight, and values in parentheses are percentages, with untreated controls as 100%.

[a] Nonsignificant; [b] $P < 0.05$; [c] $P < 0.01$.

totoxic agents [13,14]. The decreased activities of these enzymes after prolonged treatment with the condensate could be attributed to a decrease in enzyme synthesis and/or decrease in cell population and desquamation of intestinal mucosa rich in these enzymes.

Glucose 6-phosphatase is an important enzyme in carbohydrate metabolism. Its activity depends on lipids and intact membranes [13,15] and is very sensitive to hepatotoxic agents [14]. Exposure to jurak smoke condensate reduced the enzyme activity by approximately half. This could be due to the exposure of these tissues to toxic compounds which interfere with enzyme synthesis. However, the slow rate of recovery of the intestinal enzyme after withdrawal of the condensate could be due to increased desquamation of intestinal mucosa or decreased cellular degeneration.

Cholinesterases are formed in the liver. Serum enzyme activity is reduced when there is liver damage or exposure to toxic agents [16]. In the present study, a significant reduction in cholinesterase activity was observed after two or three months of treatment with the condensate, which indicates the presence of toxic substances in the jurak smoke condensate. The very slow rate of recovery suggests an irreversible binding between the enzyme and one or more components of the extract. In such cases, recovery to normal levels requires either synthesis or new enzyme molecules and/or production of new cells, and both processes are time consuming. These results confirm the previous finding of a number of potentially carcinogenic and hepatotoxic agents in jurak smoke condensate [3]. In conclusion, it appears that water filtration of jurak smoke does not remove all hazardous compounds from the smoke.

Acknowledgments

This project was supported by a grant No. 132/407 from the Science Research Committee of King Abdulaziz University, Jeddah, Saudi Arabia.

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SMOKING HABITS OF KING SAUD UNIVERSITY STUDENTS IN RIYADH

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تم استقصاء عادات التدخين لدى ٢٢٦٤ طالباً في جامعة الملك سعود. بلغت نسبة الطلاب المدخنين ٣٧٪، وكان أكثر من نصفهم يدخنون أكثر من ١٥ سيجارة يومياً. كانت السجائر هي مادة التدخين الرئيسية، وكان معظم الطلاب مدركين لأخطار التدخين من خلال وسائل الإعلام وراغبين في الإقلاع عنه. أورد غير المدخنين الوازع الديني وعدم تدخين الوالدين كأهم أسباب امتناعهم عن التدخين. وتوصي المقالة بضرورة تنظيم حملة صحية عامة للحدّ من انتشار التدخين.

The smoking habits of 2264 male students at King Saud University were investigated. Thirty-seven percent of the students smoked, and over a half smoked more than 15 cigarettes per day. Cigarettes were the main form of smoking. Most of the smokers knew about the hazards of smoking through the media and wished to stop smoking. Nonsmokers cited religious consideration and nonsmoking parents as the most important reasons for not smoking. A public health campaign is strongly recommended to reduce the prevalence of smoking.

Concern about smoking originates from its association with lung cancer, coronary artery disease, and chronic bronchitis. These diseases are still not prevalent in Third World countries, but to prevent a future epidemic of smoking-related diseases, antismoking campaigns in these countries should be started. For such campaigns to be effective, the smoking habits of the populations at risk must be defined and this has not been done for Saudi Arabia. Therefore, we have documented the smoking habits of the students in one of the biggest Saudi universities to provide baseline data.

Subjects and Methods

A sample of 2264 students was selected by taking whole classes at random from among 25,000 students entered into six colleges (Arts, Science, Engineering, Agriculture, Education, and Administration Sciences) of King Saud University, Riyadh. The Faculties of Medicine and Allied Medical Sciences were excluded because they were included in another similar survey. All these colleges are exclusively for male students. The age range was 18 to 26 years. The participants completed a questionnaire devised by the World Health Organization, consisting of questions on personal background, smoking behavior, and perception of smoking as a health hazard. The questionnaires were anonymous and the information treated in strict confidence. The questionnaires were adequately completed by 2165 students (a response rate of 96%), and the data obtained were analyzed by computer. The chi-square test was used to determine significance.

Results

Thirty-seven percent of the students were regular smokers. Of these, 58.5% started smoking above the age of 15 and 36% between 10 and 15 years (Table 1). Cigarettes were smoked by 84% and the remainder smoked either sheesha (hub-

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Accepted for publication 12 June 1990.

TABLE 1. *Age at the start of smoking.*

Age	Number	Percentage
<10	43	5.4
10–15	286	36.0
>15	464	58.5
Total	793	100

TABLE 2. *Number of cigarettes smoked daily.*

No. of cigarettes	No. of smokers	%
<10	68	10.2
10–15	219	32.9
>15	379	56.9
Total[a]	666	100

[a] 127 students smoked sheesha, pipes, or cigars.

TABLE 3. *Responses to questionnaire items.*

Response	Number	Percentage
DO YOU THINK SMOKING IS HARMFUL TO HEALTH?		
Strongly agreed	517	65.1[a]
Mildly agreed	198	24.9
Disagreed	22	2.7
No opinion	56	7.0
HAVE YOU EVER THOUGHT ABOUT QUITTING SMOKING?		
Yes	530	68.8
No	263	33.1
Total	793	100

[a] $P < 0.0008$.

TABLE 4. *Reasons for not smoking.*

Reason	Number	%
Religious	671	48.9
Nonsmoking parents	271	19.7
Self-discipline	143	10.4
Saving money	144	10.4
Others	100	7.3
More than one reason	43	3.1
Total	1372	100

TABLE 5. *Sources of information about the smoking hazards.*

Source	Nonsmokers(%)	Smokers(%)	Total(%)
School	260 (18.9)	124 (15.6)	384 (17.7)
Doctor	308 (22.4)	155 (19.5)	463 (21.3)
Media	755 (55.0)	499 (62.9)	1254 (57.9)
Others	20 (1.4)	5 (0.6)	25 (1.2)
More than one source	29 (2.1)	10 (1.2)	39 (1.8)
Total	1372	793	2165

$P < 0.0012$.

ble-bubble), cigars, or pipes. Fifty-seven percent of the cigarette smokers smoked more than 15 cigarettes daily (Table 2). Only filter-tipped cigarettes were smoked. Most smokers (65.1%) strongly agreed that smoking is hazardous to health and admitted that they would like to stop (68.8%) (Table 3). Sixty-nine percent of the nonsmokers cited religion or being brought up by nonsmoking parents as reasons for not smoking (Table 4).

The students' main sources of information on the hazards of smoking were television, press, and radio (Table 5).

Discussion

The import of cigarettes into Saudi Arabia began after 1950. Since then cigarette smoking has increased, although no figures on consumption are available.

The proportion of regular smokers in our study is similar to that reported for adults elsewhere in the Third World, where on average 40% of males are smokers. This is as high as the figures reported from some European countries [1,2]. This represents a great change for a traditional society like Saudi Arabia where until recently smoking was an unacceptable social habit. Most of the smokers had had their first smoke between 13 and 15 years of age. This is also comparable with data from other Third World countries [3,4]. Cigarettes were used by most smokers who participated in the study. Other forms of smoking, such as hubble-bubble (sheesha), though they exist in Saudi Arabia (the Western region in particular), are relatively unpopular among educated people. Only 16% of the students in this study smoked either sheesha, pipes, or cigars.

The high proportion of students who smoked despite the known risks and their desire to stop shows how difficult it is to do so once it becomes an established habit. Different surveys have shown that three of four smokers either wish or have tried to stop smoking, but only one is successful [5,6]. It is surprising that schools have played a lesser role than the media in educating university students to the ill-effects of smoking.

In view of the results of this study, we recommend that health education concerning the dangers of smoking should start at the primary school level in Saudi Arabia, as age 15 seems to be the peak age for starting. This should help prevent the start of smoking among adolescent Saudis. Religious motivation should be a part of any health education program in this country, as Islam considers smoking unlawful and distasteful. For this reason, all advertising of tobacco in newspapers, on radio, television, and posters is prohibited in Saudi Arabia. Foreign printed publications are the only sources of cigarette advertising. Sports sponsorship by tobacco companies is also not allowed. Cigarette packets carry a fairly strong health warning stating that "smoking is the major cause for cancer, lung diseases and cardiovascular diseases." However, cigarettes in Saudi Arabia are cheaper than many other places (e.g., half the price in the United Kingdom). The policy of regular increases in cigarette taxes has already been adopted in Saudi Arabia and cost is the single most effective means of discouraging cigarette consumption. Pictorial warnings on cigarette packages, in addition to written warnings, should be considered. A blurb advising smokers to refrain from smoking could be added to the health warning to give the antismoking message greater impact. Since 15 years is the crucial age for starting smoking, we recommend legislation be enacted to ban the sale of tobacco to anyone under the age of 18.

Acknowledgment

We gratefully acknowledge the help of Dr. Keith Ball.

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PATTERNS OF CIGARETTE SMOKING IN JORDAN: A STUDY OF GREATER AMMAN AREA

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تم تحديد نماذج التدخين في الأردن باستخدام عينة مكونة من ٣٤٨٩ شخصاً يمثلون طبقات مختلفة من المجتمع. وقد شملت العينة ٢١٠٣ طلاب و١٣٨٦ من غير الطلاب. كانت نسبة المدخنين لدى مجموعة غير الطلاب: ٥٨,٥٪ بين الذكور و٢٧,٤٪ بين الإناث، وعلى وجه العموم فإن ٩٦٪ منهم يدخنون سجائر مصنعة. بلغ معدل التدخين بين الذكور خمساً وعشرين سجيرة في اليوم، وبين الإناث ست عشرة سجيرة في اليوم. وكان معدل فترة التدخين لدى الذكور ٢٦ عاماً ولدى الإناث ١٣,٤ عاماً. وكانت أعلى نسبة للتدخين بين العمال المهرة وغير المهرة والأميين. أما مجموعة الطلاب فقد كانت نسبة المدخنين أعلى لدى الذكور في المرحلة الجامعية (٥٢,٩٪) وفي الكليات (٥٤,٣٪)، في حين بلغت نسبة المدخنين الذكور في المرحلة الثانوية ١٦,٧٪. وكانت نسبة التدخين بين الطالبات في المستوى الجامعي أو الكليات ٢٠,٣٪ و٩,١٪ على التوالي، فيما كانت نسبة الطالبات المدخنات في المرحلة الثانوية ٥,٤٪. وقد تبيّن أن ٩٩,٣٪ من الطلاب والطالبات يدخنون السجائر المصنعة. كان معدل التدخين لدى الطلاب الذكور ثماني عشرة سجيرة ونصف في اليوم ولمدة ٦,٤ سنوات فيما كان المعدل لدى الطالبات ٩,٦ سجيرة في اليوم ولمدة ٦,٢ سنوات. وعلى ضوء هذه النتائج، يتبين لنا مدى الحاجة للقيام بحملة مكثفة لمكافحة التدخين.

The patterns of smoking in Jordan were determined in a sample of 3489 subjects representing various strata of society. The sample included 2103 students and 1386 nonstudents. In the nonstudent population, 58.5% of the male and 27.4% of the female subjects were smokers; overall, 96% smoked manufactured cigarettes. Males smoked an average of 25 cigarettes per day, and females an average of 16 cigarettes per day. Males had smoked for an average of 16 years and females an average of 13.4 years. Smoking was highest among skilled and nonskilled workers and illiterate persons. Among students, smoking was higher in males at the university (52.9%) and college (54.3%) level; 16.7% of high school males smoked. In female students at the university or college level, 20.3% and 9.1% smoked, respectively, and 5.4% of high school females smoked. Manufactured cigarettes were used by 99.3% of the students. Male students smoked a mean of 18.5 cigarettes per day for an average of 6.4 years. Female students smoked a mean of 9.6 cigarettes per day for an average of 6.2 years. Based on our findings, it is apparent that a rigorous antismoking campaign is needed.

Cigarette smoking is considered a major public health problem in both developed and developing countries [1,2], and represents the single most preventable cause of premature death among inhabitants of the U.S. and Western Europe [1,3]. Although smoking prevalence is decreasing in the U.S. and Western Europe [3,4], it is still high and may be on the increase in most developing countries [5–8].

The burden on health services in affected countries will be tremendous once the full impact of smoking on health is felt. A substantial part of the health budget will have to be directed toward cancer care secondary to smoking, thus depriving these countries of vital resources for primary health care and preventive medicine. The aim of the present work was to study current smoking patterns in a Jordan population and determine the

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Accepted for publication 24 June 1990.

TABLE 1. *Characteristics of study population.*

	Males		Females		Total		Mean age (yr)
	No.	%	No.	%	No.	%	
NONSTUDENTS							
Housewives	–	–	224	51	224	16	39
Professionals	148	16	24	5	172	12	34
Government employees	443	47	172	39	615	44	33
Private sector and laborers	343	36	17	4	360	26	35
Others	12	1	3	1	15	1	33
Total	946		440		1386		35
STUDENTS							
University	104	14	128	10	232	11	20
College	178	23	208	15	386	18	20
High school	469	62	1013	75	1482	70	16
Others	3	–	–	–	3	–	17
Total	754		1349		2103		17

various influences. The greater Amman area (GAR) was chosen as a representative area of the Kingdom. The GAR contains 40% of the Kingdom's population and includes urban, semiurban, and rural areas.

Material and Methods

A purposive sample of 3489 subjects was selected from the GAR population, representing the various strata of society with regard to gender, socioeconomic status, educational level, job, place of residence within GAR, and whether the individual was a student or nonstudent (Tables 1,2).

A self-administered questionnaire was distributed to the study population and completed in the presence of a field supervisor. The field supervisor completed the questionnaire for illiterate subjects. Items such as gender, age, place of residence, type of job, educational level, and whether a current, ex- or nonsmoker were determined. Smokers were also asked about duration, type and quantity of smoking, age at which they started smoking, and whether any family member was a smoker.

TABLE 2. *Distribution of study population according to place of residence and sex.*

	Males		Females		Total	
	No.	%	No.	%	No.	%
NONSTUDENTS						
Urban	721	76	264	60	985	71
Semiurban	58	6	149	34	207	15
Rural	167	18	27	6	194	14
STUDENTS						
Urban	618	82	1171	87	1789	85
Semiurban	76	10	114	8	190	9
Rural	60	8	64	5	124	6

Frequency distribution and cross tabulations of various study variables were done (Table 3,4). Between-group comparisons of the smoking rates were done and tested using the gaussian Z statistic [9]. Differences in the number of cigarettes smoked and duration of smoking between sexes were tested using the two-tailed t test.

Results

Among the nonstudent population, 49.1% were smokers; 58.8% were male and 27.4% were female ($P < 0.0001$). Sixteen percent of the entire student population smoked, and this constituted 30.8% of the male and 7.4% of the female students.

Manufactured cigarettes were smoked by 96% of the smokers in the nonstudent population and 99.3% of the student population. The remaining

Table 3. *Prevalence of smoking according to occupations in nonstudents and level of education in students.*

	Males		Females		Total	
Category	No. of smokers	%	No. of smokers	%	No. of smokers	%
NONSTUDENTS						
Housewives	–	–	65/224	29	65/224	29
Professionals	70/148	47	5/24	21	76/172	44
Government employees	239/443	54	34/172	20	301/615	49
Private sector and laborers	240/343	70	16/17	94	255/360	71
Total	549/946	58.0	120/440	27.3	697/1386	50
STUDENTS						
University	55/104	53	26/128	20	81/232	35
College	98/178	55	19/208	9	117/386	30
High school	80/469	17	51/1013	5	131/1482	9
Total	233/754	31	96/1349	7	329/2103	16

subjects in the two groups smoked handmade cigarettes containing *Hishi* (local tobacco).

In the nonstudent group, males smoked a mean (± SD) of 25 ± 15.9 cigarettes per day and females 16 ± 15 cigarettes per day ($P < 0.0001$). Males had smoked for 16 ± 14.1 years and females for 13.4 ± 9.1 years, but this was statistically insignificant. Among the students, males smoked a mean (± SD) of 18.5 ± 17.1 cigarettes per day and females 9.6 ± 7.1 cigarettes per day ($P < 0.0001$). Male students had smoked for 6.4 ± 5.4 years and females for 6.2 ± 3.6 years ($P < 0.01$).

In the nonstudent group, smoking was more common among males than females (58.8% versus 27.4%; $P < 0.0001$). Males smoked an average of 25 ± 15 cigarettes per day, and females, 16 ± 16 cigarettes per day ($P < 0.0001$). Males had started smoking at the mean age of 19 ± 8.3 years and females at 20 ± 9.5 years ($P < 0.0002$).

Among the nonstudent population, 71.4% were illiterate and this was significantly different from the 49.4% ($P < 0.0008$) observed for subjects with a university degree as well as those with a college degree (44.9%; $P < 0.0003$), secondary school education (43.2%; $P < 0.0002$), or intermediate school education (55.6%; $P < 0.03$). Significant differences were not observed in the number of smokers regardless of educational level. The mean age for each of these populations was similar. The influence of the type of job on smoking in the nonstudent group is shown in Table 3.

Table 4. *Prevalence of smoking in student population according to education level.*

	Percentage of smokers	*P* value
University vs	34.9	
College	30.1	NS
High school	9.0	<0.0001
College vs	30.1	
High school	9.0	<0.0001

NS = nonsignificant.

More male students smoked than did females (30.8% versus 7.4%; $P < 0.001$), and this was evident for all education levels. The two populations were controlled for age. University students and college students constituted significantly more of the smoking group than did high school students ($P < 0.0001$) (Table 4). Among smoking students, there were more fathers who smoked ($P < 0.04$) but a similar association was not seen for smoking siblings or mothers.

Discussion

To effectively mount an antismoking campaign that reaches the attention of high-risk groups, reliable estimates of smoking prevalence are needed and the factors influencing it. Significantly more adult males smoke then do their female counterparts ($P < 0.0001$), and men tend to have been smoking for longer, though this did not achieve statistical significance. Other factors beside gender were also associated with a higher prevalence, including illiteracy, being a nonskilled or skilled worker, and working in the private sector.

The smoking prevalence among adult men in our population is similar to that observed for adult men in the U.S. and England in the 1950s [3,10]. Prevalence among adult women is similar to that seen in adult American women for 1985 [4]. The majority of smoking females worked in the private sector. This may be real or an artifact resulting from the small sample size.

Smoking was more common in students whose fathers were smokers ($P < 0.04$).

Our study shows that smoking prevalence increases steadily with age in the student population, with an alarming increase occurring beyond high school (Tables 3,4).

Among the nonstudent population there were significantly more illiterates who smoked than educated subjects, regardless of the level of education. Subjects who had a higher level of education tended to smoke less but this did not reach significance. This contrasts with the findings of Pierce et al [11] in the U.S. who reported that a higher educational level was important in decreasing the overall prevalence of smoking.

Based on our findings, it is apparent that a rigorous campaign is needed in Jordan to reduce the high prevalence of smoking.

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DYNAMIC COMPUTED TOMOGRAPHY OF CEREBRAL CIRCULATORY ARREST

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إن توقف دورة الدم في المخ هو النظير الوعائي الفيزولوجي لموت الدماغ. ظهر ركود الدم في الأوعية الكبرى في قاعدة الدماغ وانعدام التروية الشامل لأنسجة الدماغ في المستوى المقطعي بما في ذلك نصفي كرة الدماغ وجذع الدماغ والمخيخ وذلك في ثمانية حالات متتابعة لمرضى شخصت لديهم وفاة الدماغ سريرياً وكانت ناجمة عن أسباب مختلفة. وبينما يعتبر التأكد السريري من موت الدماغ إلزامياً، فإن هذه الدراسة تثبت أن مسح القحف الطبقي الدينمي بالحاسوب بعد الحقن الوريدي للمادة الظليلة يعتبر أسلوباً فعالاً، وغير باضع وقد يفيد في إجراء التقييم الفوري للشذوذ الشامل في التروية القحفية وهو المميز لهذه الحالة.

Cerebral circulatory arrest is the physiological vascular equivalent of brain death. A series of eight consecutive patients referred with a clinical diagnosis of cerebral death secondary to various causes exhibited stagnation of blood within major vessels at the base of the brain, and complete gross nonperfusion of cerebral tissue within the plane of section, to include the cerebral hemispheres, brainstem, and cerebellum. While clinical confirmation of brain death is mandatory, this study confirms that intravenous dynamic cranial computed tomography is an efficacious, noninvasive method that may be useful in the immediate evaluation of the generalized abnormal cranial perfusion peculiar to this condition.

Cerebral circulatory arrest (CCA) has been evaluated by numerous conventional radiological methods as well as by computed tomographic (CT) techniques [1–17]. While final clinical confirmation of any diagnostic radiological procedure is mandatory, initial noninvasive radiological techniques may be valuable. This study was undertaken to evaluate the potential usefulness of intravenous dynamic cranial computed tomography (IVDCT) to elucidate the abnormal patterns of perfusion within the cerebral parenchyma and major cranial vessels associated with "brain death."

Material and Methods

A total of eight patients who were referred with no evidence of electrical activity on prior electroencephalographic (EEG) determinations and a clinical diagnosis of brain death [18] were studied with IVDCT using a GE-9800 CT scanner (Table 1). A standard injection sequence was used: 4 ml of Renografin-76 per second injected through a 20-gauge antecubital venous catheter, for a total of 60 ml. A contrast dose per weight reduction in these parameters was made for pediatric patients. The scan sequence was also standardized: one initial scan followed by an 8-second arm-to-head circulation time delay, 12 scans in rapid sequence without interscan delay (approximately 4.5 sec/scan), and 8 subsequent scans with a 30-second interscan delay. This extended the sequence through approximately 5 minutes. The study was performed at one level, with a 5-mm section thickness, through the suprasellar cistern. Time–density dynamic perfusion curves were constructed on each patient for the entire 5-minute sequence.

A control series of five subjects was included for comparison with the test results. No adverse reactions nor complications attributable to the procedure were encountered.

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Accepted for publication 27 March 1990.

TABLE 1. *Clinical cause of brain death.*

Cause	No.
Postoperative hypoxia	2
Asphyxia/drowning	2
Trauma	2
Spontaneous cranial hemorrhage	1
Bacterial meningitis	1

Results

Control subjects who underwent IVDCT demonstrated normal time-density curves. This included the expected regional wash-in, peak, and wash-out of the contrast medium (Figure 1).

In the test subjects, the actual contrast-enhanced cerebral vessels on IVDCT sequences, if observed at all (six patients), were remarkably attenuated in both size and density. As compared to control subjects, the dynamic perfusion curve evaluation of subjects with clinical CCA demonstrated a reverse ratio between the measurements of the external carotid peak density and the peak density of the major components of the circle of Willis (Figure 2). In normal circumstances, the vessels of the circle of Willis always revealed a perfusion peak amplitude which was higher than that of the external carotid system. In addition, in six of eight patients with CCA, the plateau phase of the dynamic perfusion curve continued to rise with a broad perfusion base, or even absence of wash-out, indicating that the contrast (i.e., blood) in the major vessels supplying the cerebrum was stagnant (Figure 2). Two subjects showed absolutely no evidence of the arrival of contrast within intracranial vessels, either visually or by dynamic perfusion curve determinations (Figure 3).

Most importantly, measurements of the volume of cerebral tissue itself within the plane of section revealed no evidence of a rise of CT density above baseline in any of the eight subjects (Figure 3). This indicates that no intravascular contrast (i.e., blood) perfused the cerebral tissue being imaged during the 5-minute acquisition sequence.

A simple check of the proficiency of the contrast injection was performed by the simultaneous visual monitoring of the arteries and veins in the scalp, which are supplied by the external carotid artery. These vessels are not subject to the same effects imposed on the intracranial vessels in the pathological state of CCA, and therefore their perfusion is normal (Figure 2).

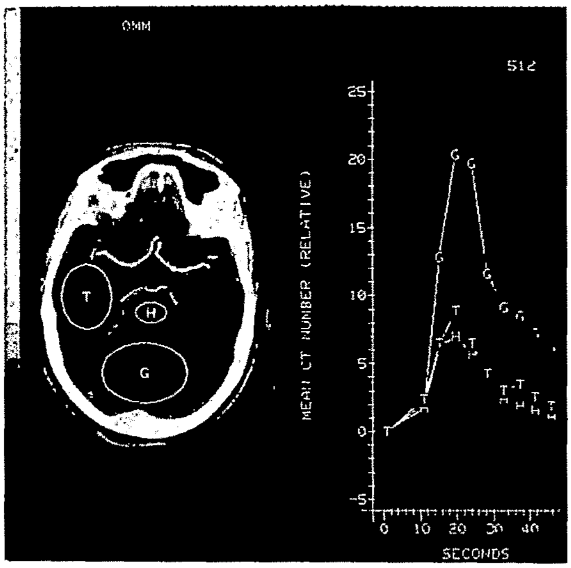

FIGURE 1. Dynamic time-density curves in a normal subject, demonstrating the expected regional wash-in peak, and wash-out in the brainstem *(H)*, cerebellum *(G)*, and right temporal lobe *(T)*.

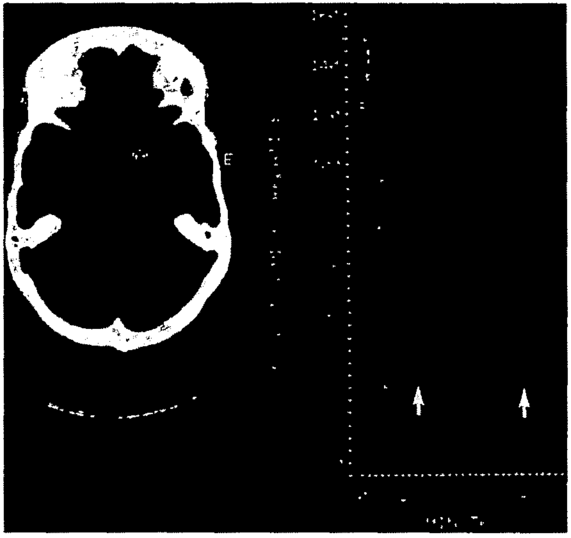

FIGURE 2. Dynamic time–density curves through 5 minutes revealing normal perfusion in the left superficial temporal artery *(E)*, which far exceeds the circulation in the internal carotid artery *(A)*. This represents a reversal in the normal perfusion characteristics in these two structures. In addition, the internal carotid demonstrates an elevated plateau phase that is nearly equal to the wash-in peak, indicating no significant "wash-out" of contrast, and therefore stagnation *(arrows)*.

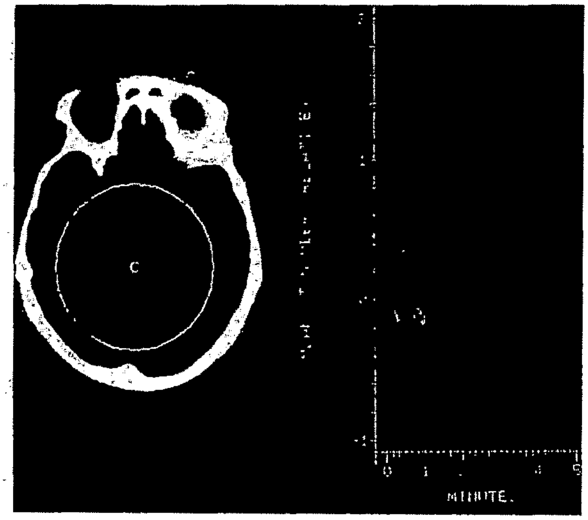

FIGURE 3. Dynamic time–density curve through 5 minutes, demonstrating a completely flat "curve" indicating no evidence of flow of contrast (i.e., blood) into the cerebral tissue *(C)*.

Discussion

The findings on IVDCT in CCA are in some ways more straightforward and in other ways more complex than past reports would indicate [19–22]. CT is sufficiently contrast sensitive to detect minor amounts of intracranial intravascular contrast media that would be otherwise missed during conventional angiography. This study indicates that, in many cases of clinical brain death, contrast media seems to reach the vessels at the base of the brain by slow, pulsatile percolation which is too slow and quantitatively too small to be physiologically meaningful. However, the major observation is not the appearance of the major cerebral vessels themselves, but the degree of perfusion of the cerebral parenchyma served by these vessels. In every case, the visualized cerebral substance showed no evidence of the arrival of measurable vascular iodinated contrast material. This is the IVDCT equivalent of clinical brain death in cases of CCA. As this is a pilot study, additional studies are required to evaluate other causes of deep coma that may be potentially reversible.

In any case, cerebral injury with concomitant progressive expansion of the brain within the relatively closed space of the cranial vault, if unchecked, eventually reaches a state of irreversibility. The intracranial pressure eventually reaches that of the mean arterial systolic systemic blood pressure in spite of the regulatory "Cushing" effect. Any clinical pressure increase above this level causes a halt in the flow of blood into the intracranial space. This is the threshold at which CCA is reached, and within minutes, all nonperfused cerebral parenchyma not already injured will be irreversibly ischemically damaged. At this time a state of clinical cerebral death exists. IVDCT certainly cannot absolutely ascertain cellular death; however, without vascular perfusion, the rapid demise of cerebral tissue is assured. In fact, for several minutes before anoxic cell death occurs, CCA will actually precede this complete terminal ischemic neural process.

IVDCT therefore provides a fast, safe technique that is simple to perform in subjects with CCA. It yields important information regarding the status of gross cerebral parenchymal perfusion which is missing from static pre- and postcontrast CT examinations. In selected cases it may be a useful adjunct to the integrated clinicoradiological evaluation of patients with suspected brain death, thereby replacing less sensitive, invasive neurodiagnostic procedures [8].

Acknowledgments

I wish to thank Joanne Murray for the manuscript preparation, C. Jinkins for the manuscript research, and the K.F.S.H. Radiology Department for assistance with the illustrations.

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GASTROESOPHAGEAL REFLUX IN INFANTS AND CHILDREN

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يعتبر الجزر المعدي المريئي اضطراباً مألوفاً لدى الولدان والرُضع في سائر أنحاء العالم. يهدف هذا المقال إلى توفير المعلومات المستجدة ذات العلاقة بمختلف أنماط هذا الداء. نأمل أن تؤدي هذه الدراسة إلى زيادة الوعي وإلى تنشيط الأبحاث في هذا المجال.

Gastroesophageal reflux is a common disorder in infants and children worldwide. This paper is intended to provide updated information on various aspects of the disease. It is hoped that this review will increase awareness and stimulate research in this field.

Gastroesophageal reflux (GER) is a common condition in infants and children. The availability of more sensitive diagnostic techniques has increased awareness and recognition of reflux. Consequently, better understanding of its pathogenesis, clinical manifestations, and complications has improved patient care.

Despite worldwide interest in GER, no reports have originated concerning its pattern in Saudi Arabia though the problem does exist here. In a five-year retrospective survey, we documented 22 cases of GER, of which six (27%) had peptic esophagitis [1]. This incidence of four to five cases per year is a conservative figure, considering the limited diagnostic facilities at our institution. Nevertheless, these data strongly suggest that GER is not uncommon in the pediatric population of Saudi Arabia. We will discuss the various aspects of GER in children that may contribute to early recognition and management of this disorder.

In 1959, Carre [2] estimated an incidence of gastroesophageal reflux (GER) of 1000 live births, but has since revised this estimate to approximately 1 in 300 live births [2]. A similar increase has been noted for many centers in Europe and North America, but this is attributed to increased awareness and recognition of the disease as a result of the availability of more sensitive diagnostic techniques, rather than to a true increase in the incidence of GER [3]. A male preponderance of about 60% has also been reported in most studies. There is also a higher incidence of GER in patients with certain disorders. These include congenital disorders of the nervous system, mental retardation, and Down's syndrome [4]. Similarly, recurrent respiratory symptoms and anastomotic strictures commonly develop in infants who have been operated on for esophageal atresia and tracheoesophageal fistula. These problems result from GER and associated motility disorders of the esophagus [5].

Knowledge of the natural history of any condition is essential. The indications and different approaches to treatment must be weighed against the outcome if no therapy is used. In England, Carre reported that most infants have symptoms by two months of age, and that 60% of the patients will be symptom-free by 18 months of age, with the greatest improvement occurring by eight to ten months when most infants assume an upright posture. However, the same author pointed out that, if untreated, about 30% of the patients will continue to have symptoms up to four years of age, 5% will die, and esophageal strictures will develop in another 5% of the patients, requiring extensive medical and surgical treatment [6].

Pathogenesis

Although the mechanism of GER is not fully

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Accepted for publication 4 April 1990.

understood, several anatomic and physiological features appear to be important in the prevention of reflux. These include the supportive role of the phrenoesophageal ligament, the acute esophageal angle contributing to a flap valve mechanism, and the role of the basal lower esophageal sphincter (LES) pressure.

The LES, which is an extension of the esophageal muscle, has no anatomic identity. However, the sphincter muscle differs from the esophageal muscle in its greater response to cholinergic stimulation. In addition, the LES (with its positive resting pressure of 15 to 60 mm Hg) is located between the stomach (with its positive pressure of 6 to 10 mm Hg) and the intrathoracic esophagus (with its negative pressure of –6 to –10 mm Hg) and constitutes a true barrier that gastric contents must overcome in order to reflux into the esophagus [7]. However, it is well known that the LES pressure is variable, as the sphincter undergoes spontaneous relaxations that are independent of relaxations triggered by deglutition [8].

Earlier reports suggested that most patients with reflux have reduced basal LES pressure as compared with normal subjects [9,10]. However, overlaps between normal subjects and patients with GER have been seen. Furthermore, recent studies using simultaneous and continuous esophageal manometry with pH monitoring have shown that, in patients with GER, only 12% of the reflux episodes occurred while the resting LES pressure was reduced, and the majority of reflux episodes (54%) occurred during transient increases in intraabdominal pressure associated with physiological activities such as coughing, crying, defecating, and moving about of patients who were awake [8,11]. It would appear that the role of reduced resting LES pressure has been overestimated in earlier reports, and the role of other factors in the genesis of GER should be studied. Finally, the delayed gastric emptying commonly seen in patients with GER and which is most marked in infants with pulmonary disease, makes it a potentially important factor in the pathogenesis of reflux [12].

Regardless of its mechanism, the reflux of gastric contents (hydrochloric acid, bile acids, pepsin) into the esophagus has severe pathological consequences. These substances damage esophageal mucosa, resulting in peptic esophagitis. The incidence and severity of esophagitis depends on the criteria of diagnosis, the type of refluxed material, and the efficiency of esophageal clearance. Delayed acid clearance with or without abnormal esophageal peristalsis has been found more commonly in patients with GER and esophagitis than in normal controls [13,14].

Respiratory manifestations of GER may result from aspiration or from the reflex mechanism. Recurrent pneumonia [15], chronic bronchitis [16], and near-miss infant death syndrome [17] have been associated with GER and repeated aspiration. However, the presence of acid in the lower esophagus, without evidence of inhalation, has been implicated in the genesis of reflex laryngospastic disorders such as obstructive apnea, sudden infant death syndrome, and stridor [18-20]. Similarly, bronchospastic episodes such as nocturnal asthma and cough in patients with GER have been linked to a reflex mechanism, rather than to aspiration [15,21]. Although there is strong evidence implicating GER in the genesis of respiratory distress, this relationship is more complex. Conditions associated with increased positive intraabdominal pressure, such as coughing and wheezing, may themselves induce GER. Other disorders causing increased negative intrathoracic pressure, such as hiccups and stridor, may also potentiate GER. Furthermore, therapeutic modalities such as bronchodilators, nasogastric tubes, and chest physiotherapy, which are frequently used in patients with respiratory disease, may induce reflux by a variety of mechanisms. The interrelationship between GER and respiratory disorders therefore remains obscure and needs further investigation.

Clinical Manifestations

The clinical presentation of patients with GER has been described in the literature. Vomiting is the most common symptom in infants and children, occurring in about 90% of cases. The projectile type is not uncommon, and may be confused with pyloric stenosis or pylorospasm. When vomiting is severe, it leads to loss of water, electrolytes, and calories, causing dehydration with electrolyte imbalance, failure to thrive, and malnutrition. Respiratory manifestations have already been mentioned. Patients with recurrent pneumonia, reactive airway disease, chronic nocturnal cough, recurrent stridor, bronchopulmonary dysplasia, and apnea, as well as those with near-miss sudden infant death syndrome, may have GER and should be investigated for this possibility, even if there is no history of vomiting. Irritability in infants, heartburn in older children, melena or hematemesis, and iron-deficiency anemia are well-known manifestations of peptic esophagitis complicating GER. Unusual clinical features include Sandifer syndrome, abnormal posturing, and movements simulating convulsions, rumination, and protein-losing enteropathy. All of these manifestations disappear once appropriate therapy for GER is introduced.

Diagnostic Methods

The number of diagnostic tests have been increasing, which indicates that no single test is able to distinguish all patients with significant GER from those with physiological reflux. The fact that reflux of gastric content into the esophagus occurs in nearly all normal subjects [22] and the scarcity of data on patterns of physiological reflux in healthy pediatric patients have made it difficult to define clinically significant GER. Nevertheless, the development of newer techniques, such as prolonged esophageal pH monitoring, has not only increased the ability to diagnose significant reflux but also to relate reflux episodes to a variety of clinical conditions.

Barium swallow

Barium swallow is one of the oldest methods used to diagnose GER. Its most important advantages are availability, technical simplicity, and the ability to detect swallowing and structural abnormalities, as well as esophagitis with strictures that may be associated with reflux. Disadvantages include a high incidence of false-positive and false-negative results. However, recently developed radiological techniques may enhance the radiologist's skill in detecting significant reflux [23]. Although there are no clear-cut criteria for the diagnosis of reflux in barium studies, it is generally accepted that small, brief wisps of barium reflux are insignificant and should not be overinterpreted. By contrast, reflux occurring more than twice during brief fluoroscopy, or reflux with clear delay in esophageal clearing, is strongly suggestive of GER.

Scintigraphy

Scintigraphy involves the administration of a meal labeled with a radionuclide agent (technetium 99m), given either orally or by nasogastric tube, and scanning of the esophagus for evidence of reflux. The ability of this study to detect the immediate postprandial reflux, bile reflux, and pulmonary aspiration is one of its most important advantages. However, the presence of radioactive material in the lung fields does not necessarily prove aspiration caused by GER; it can also have occurred during swallowing. Other advantages of the scintiscan include the ability to diagnose and treat delayed gastric emptying [24].

Esophageal pH studies

These tests directly measure esophageal pH and therefore can detect acid and, more rarely, alkaline reflux into the lower esophagus. The duration of monitoring is variable according to the information required.

The Tuttle test (acid reflux test) was originally used in adults and has been modified for pediatric patients [25]. It involves the instillation of 300 ml of 0.1 NHC1/1.73 m^2 into the stomach to ensure a low gastric pH. A pH probe placed about 3 cm above the LES measures changes in esophageal pH, which is monitored for about 30 minutes. The test is positive when more than one episode of reflux ($pH < 4$) occurs in 30 minutes, or when a single episode lasts for more than 30% of the monitoring time. Unsweetened apple juice may be used instead of HCl. The test is simple, and accuracy may reach 85% [25]. As with any test, false negative and false positive results can occur.

The Tuttle test monitors esophageal pH for brief periods and produces high false-negative results. Monitoring esophageal pH for three to six hours has therefore been suggested. The variables that are usually analyzed are: the number of reflux episodes ($pH < 4.0$), their duration, the number of episodes more than five minutes long, the duration of the longest episode, and the percentage of time the pH is less than 4.0. The method remains relatively simple, and when performed on fasting, supine, sedated patients, it is sufficiently accurate to diagnose reflux in most cases [26].

Extended or prolonged monitoring of esophageal pH is usually performed continuously for 18 to 24 hours [27]. The pH probe is placed in the same way as for the acid reflux test, and the variables analyzed are the same as those for the shorter tests. The more prolonged study time also permits recording of other events, such as the position of the patient, sleep or waking state, meals and administration of drugs, all of which may affect the number and duration of reflux episodes [28,29]. Furthermore, the relationship between reflux and other disorders, such as apneic and bradycardic episodes and sleep disturbances, may be defined by this method, in conjunction with other polysomnographic studies [30,31]. The need to hospitalize patients for performing extended pH studies has been obviated by the recent development of portable pH recorders that are programmed to measure pH levels every one to sixty seconds with a built-in event marker. Recent studies have indicated age-related differences in the variables obtained from the test. Younger infants tended to have fewer and shorter episodes of reflux, with a gradual increase with increasing age [28]. Other studies have shown that the frequency and duration of reflux episodes when patients are upright or awake are similar for patients with GER and controls. During sleep (recumbent position), significant differences are demonstrable [32]. Further studies on portable pH monitoring are needed to define the normal range of pH parameters for ambulatory infants and children, and the relationship of GER to associated disorders.

Esophageal manometry measures the pressures generated by the esophageal musculature using perfused catheters that are introduced into the stomach and pulled out slowly. Despite earlier technical difficulties, this test, especially when coupled with pharyngeal electromyography, gives valuable information on the function of both the lower and upper esophageal sphincters, as well as the motility of the esophagus. The position and pressure of the LES can be defined in the resting state and during deglutition. However, motility disorders may be the cause or the result of GER. Therefore, esophageal manometry, though not considered a diagnostic test for reflux, is a useful adjunct in the evaluation of these patients [33].

Endoscopy and biopsy are also used in the diagnosis of GER. The principal advantage of endoscopy is the demonstration of esophagitis that frequently complicates GER. The fact that peptic esophagitis can occur without gross endoscopic findings indicates the necessity for biopsies, even though the mucosa may appear normal [34].

In the Bernstein test, saline and 0.1 NHC1 are alternately administered to the esophagus by drip through a nasogastric tube. The patient, who does not know which solution is being infused, is asked whether he or she feels any symptoms, usually heartburn. The study is of limited value in infants and children who are unable to describe symptoms. Its greatest value, in older children and adults, is the ability to demonstrate the association of atypical symptoms and GER and to differentiate esophageal pain from other causes of chest pain.

Therapeutic Methods

Although LES pressure is not clearly modified by positioning, esophageal pH studies have demonstrated significant variation with position. The number of episodes and the percent time of the episode are more important in the wakeful than in the sleeping state. Furthermore, in the awake state, the number of reflux episodes was found to be less frequent in the upright than in the recumbent position [32]. Moreover, it is generally accepted that the prone position is more effective than the dorsal position, probably because it facilitates gastric emptying. Therefore, positioning in ventral decubitus (prone position) with a 30- to 45-degree inclination angle, 24 hours a day, is recommended for the success of postural therapy [35].

With regard to the dietary measures, recent studies have indicated that the efficacy of adding a thickening agent, such as rice cereal, to infant feeds varies from unpredictable to beneficial. However, it is generally accepted that thickening the infant's liquid meals with cereal is not only harmless but also provides more calories in the diet. Small, frequent feedings avoid overfilling of the stomach. In older children, reduced intake of fat and chocolates and avoidance of exposure to tobacco smoke are based on the adverse effects of these factors on the LES pressure.

Drug therapy represents an additional approach to the medical treatment of GER. Antacids neutralize hydrogen ions in the stomach and protect the esophageal mucosa from the effects of acid reflux. These drugs are effective in the treatment of esophagitis and relief of heartburn. The presence of simethicone, dimethicone, or alginates may be additionally protective [36,37]. The usual dose of aluminum and magnesium compounds is 30 to 60 ml/1.73 m^2/day.

H_2 antagonists, such as cimetidine inhibit gastric acid secretion and therefore may help in the treatment of esophagitis [38]. The usual dosage is 30 to 40 mg/kg/day. The drug has potentially serious side effects, however, and should not be considered for prolonged use in children. Newer, more potent H_2 blockers, such as ranitidine and famotidine, with reportedly fewer side effects, might replace cimetidine in the treatment of esophagitis.

Prokinetic agents are also used in the treatment of GER. Metoclopramide is a dopamine antagonist. It increases the LES pressure, increases the amplitudes of smooth muscle contractions, and coordinates gastric, pyloric, and duodenal muscle activity [39,40]. The usual dosage is 0.3 to 0.5 mg/kg/day. However, the drug has been associated with serious side effects such as methemoglobinemia in young infants, extrapyramidal syndromes, sedation, dizziness, and restlessness.

Unlike metoclopramide, domperidone does not readily penetrate the central nervous system and therefore is less likely to cause extrapyramidal side effects. The prokinetic actions of domperidone are, however, similar to those of metoclopramide. Domperidone is considered more potent but with fewer side effects [41,42]. The usual dosage to achieve a prokinetic effect is 0.3 to 1 mg/kg/day.

Bethanechol is a stable choline that is not hydrolized by acetylcholinesterase. It increases the LES pressure, but its action appears to be related more to improved esophageal motor activity and clearance, rather than increased LES or gastric emptying [43]. Studies in patients with reflux indicate that this drug is effective in decreasing the frequency and duration of reflux episodes. However, a recent study comparing bethanechol and aluminum hydroxide found that both drugs are equally effective in reducing the number of reflux episodes and clinical symptoms [44]. The average oral dosage is 0.6 mg/kg/day, divided into three doses. Side effects may include headache, abdominal pain, and increased blood pressure.

Cisapride is believed to affect gastrointestinal function through indirect cholinergic mechanisms without interfering with dopamine receptors [42]. When used in patients with GER, the drug was observed to not only decrease all esophageal pH monitoring parameters but also improved esophageal peristalsis, leading to improved clinical symptoms [42]. The usual oral dosage is 0.2 mg/kg, given three to four times daily. Side effects include abdominal cramps, diarrhea, disorders of appetite, and somnolence.

Surgical Therapy

The most commonly used surgical technique is the Nissen fundoplication, followed by Thal fundoplication and gastropexy. Pyloroplasty alone or in combination with fundoplication may be required in some patients who have marked delay in gastric emptying [45]. The outcome of surgical therapy is excellent. Reflux is cured in about 95% of cases, and mortality varies from 0 to 0.5%. Surgery is less effective in mentally retarded patients with GER, however, and most deaths occur in patients who have additional high-risk factors such as prematurity or congenital heart disease [46,47]. In addition, the complications of surgery, including the gas bloat syndrome, are very rare.

General Approach To Treatment

Although the natural history of GER indicates that the condition of most infants improves with age, spontaneous recovery is impossible to predict. Therefore, all patients with significant GER should be treated. Except in the event of life-threatening manifestations, an adequate trial of medical treatment should be given, consisting of postural therapy with the patient in the prone position at a 30-degree caudal inclination for 24 hours a day, thickening of liquid feeds with dry rice cereal, and the use of a prokinetic agent. This regimen should be followed for six to eight weeks. Antacids and H_2

blockers should be reserved for patients with esophagitis, although some practitioners routinely prescribe antacids. The duration of treatment in patients who respond is controversial. We recommend continuing the same regimen for an additional two months, then decreasing the intensity of treatment, especially postural therapy, which is difficult to enforce as infants grow. If there is no improvement after an adequate trial of medical therapy, the patient should be re-evaluated and surgical therapy considered.

Surgery, without a prior trial of medical therapy, is indicated in patients with hiatal hernia and reflux. It is also recommended for infants with acute life-threatening complications, once the causal relationship between GER and such complications (apnea, near-miss sudden infant death syndrome) is established. In addition, surgical repair should be performed in patients with esophageal strictures, older infants with peptic esophagitis, patients with neuropsychiatric manifestations, and all patients who do not respond to medical therapy.

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ALPHA-1-ANTITRYPSIN PHENOTYPES IN SAUDI ARABIA: A STUDY IN THE CENTRAL PROVINCE

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أجريت هذه الدراسة على ٢٠٤ عينات من البلازما تم الحصول عليها من مواطنين سعوديين يعيشون في المنطقة الوسطى من المملكة لتحديد نسبة انتشار الأنماط الظاهرية لبروتين ألفا ١- مضاد التربسين بواسطة التبئير الكهرساوي (متساوي التكهرب) على هلامات أمفولين (ب هـ ٤-٥). كانت نسبة انتشار كل من SZ, MZ, MS, PiMM و ZZ على التوالي ٠,٨٦٧٦، ٠,٠٩٣١، ٠,٠٢٤٥، ٠,٠٠٩٨ و٠,٠٠٤٩. كما كانت التواترات الجينية لمتغيرات بروتين ألفا ١- مضاد التربسين (متغيرات PiZ, PiS, PiM) على التوالي ٠,٩٢٦٥، ٠,٠٥١٥ و٠,٠٢٢. ونقوم بوصف نتائجنا في جمهرة سعودية ومقارنتها مع النتائج المسجلة لجمهرات أخرى.

This study was conducted on 204 plasma samples obtained from Saudis living in the central province of Saudi Arabia, to determine the prevalence of alpha-1-antitrypsin (α1AT) phenotypes. The α1AT phenotypes were separated by isoelectric focusing on ampholine gels (pH 4–5). The prevalences of PiMM, MS, MZ, SZ, and ZZ were 0.8676, 0.0931, 0.0245, 0.0098, and 0.0049, respectively. The gene frequencies of the α1AT variants, i.e., PiM, PiS and PiZ, were 0.9265, 0.0515, and 0.022, respectively. We describe and compare our results in a Saudi population with those reported for other populations.

Alpha-1-antitrypsin (α1AT) is a protease inhibitor that accounts for almost 90% of the trypsin-inhibiting capacity of the serum. It has broad specificity and, besides inhibiting trypsin, it can inactivate chymotrypsin, elastase, thrombin, plasmin, and bacterial proteases [1]. The protein displays a high degree of genetically determined heterogeneity which was first demonstrated by Fagerhol and Braend in 1965 [2]. It is referred to as the protease inhibitor (Pi) system, and more than 40 Pi variants have been demonstrated in different populations and with a variable prevalence [3,4]. The most common form is PiM, which exists in most populations at frequencies ranging from 0.8798 to 0.9958 [5]. Other common variants include PiS, PiZ, and PiF [6,7].

Several studies conducted in a number of populations have shown that gene frequencies of Pi variants vary for different racial groups, but, to the best of our knowledge, no studies have been done on the Saudi population. We therefore undertook to identify the α1AT phenotypes and determine the gene frequency in a population of subjects from Riyadh in the central province of Saudi Arabia. We also compared our findings with those reported for other populations.

Material and Methods

Blood samples (1–2 ml) were collected from male and female (4:1) adult subjects seen at outpatient clinics at King Khalid University Hospital, Riyadh, (Figure 1) for various minor problems (i.e., eye testing, dental problems, wound dressing, or immunization). Hematological variables were analyzed using a Coulter counter ZF6; the

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Accepted for publication 26 March 1990.

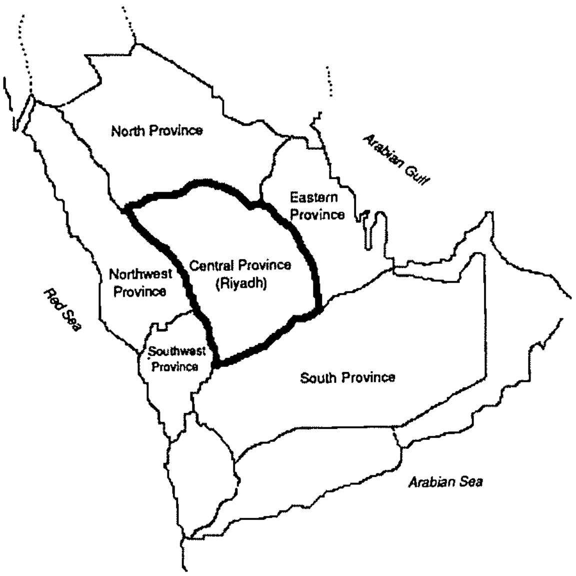

FIGURE 1. Map of Saudi Arabia showing the Central Province, where this study was conducted.

cells were separated by centrifugation and the plasma stored frozen at –20°C until required for analysis. Biochemical parameters were estimated using Autoanalyzer American Monitor.

α1AT phenotyping was done by isoelectric focusing with carrier ampholytes in 0.5-mm-thick flat-bed polyacrylamide gels. (LKB ampholine PAG plates, pH 4-5 cat. no. 1804-111; LKB-Producter AB, Sweden). Isoelectric focusing was performed on an LKB Multiphor with the cooling plate set at 10°C. The electrolyte solution consisted of 1 mol glycine for the cathode and 1 mol phosphoric acid for the anode. Sample application strips were saturated with serum samples and applied about 1 cm from the cathode end. Isoelectric focusing was carried out at 1400 V, 50 mA, and 30 W for 1 hour, following which the sample wicks were removed and the electrofocusing was continued for 2 more hours. The gel was fixed in 115.0 gm/L of trichloroacetic acid solution containing 34 gm/L of sulfosalicylic acid, stained with 1.15 gm/L Coomassie brilliant blue R 250 for 10 minutes, destained in ethanol:acetic acid:water (50:15:134), and covered with plastic preserving sheets.

Results

The results of biochemical and hematological parameters in these subjects were in the normal range and no other abnormality was apparent. Using ampholine PAG plates (pH 4–5] for isoelectric focusing, the α1AT phenotypes PiM, PiZ, and PiS were identified in both the homozygous and heterozygous states and the prevalence of the phenotypes is presented in Table 1. PiM was the normal α1AT phenotype existing in both the homozygous and heterozygous states and associated with PiS and PiZ variants. One case homozygous to the Z variants was identified. Table 2 shows a comparison of our findings in the Saudi population with those for other populations.

Discussion

We examined the α1AT phenotype frequency in the Saudi population, and found that deficient variants (i.e., PiS and PiZ) exist in both the heterozygous and homozygous states. PiM is the most common in all populations (see Table 2), and this holds true for the Saudi population as well, with a frequency of 0.9265.

The highest frequency of the PiS allele (0.1124) has been reported in the Spanish population [8], followed by 0.0713 in the French [9] and our finding of 0.0515 in the Saudi population of the central province. This is similar to that reported for the British population [10], but is lower than that cited for Spanish, French, Portuguese [11], and Italian [12] populations. Among the Afrikaner population of Southern Africa, a PiS gene frequency of 0.049 was reported [13]. The frequency of PiS in Saudis is considerably higher than that reported for several European countries (see Table 2).

The PiZ variant was encountered at a gene frequency of 0.022, which is higher than that reported for other populations, which was around 1% in most cases (see Table 2). This finding requires more extensive studies of Saudi population to identify the clinical consequences of PiZ and other variants particularly associated with liver disease, which occurs at a high frequency in Saudis.

Our investigation has shown that α1AT polymorphism exists in the Saudi population and further confirms previous suggestions that significant geographical variations in α1AT phenotypes exist among different populations. Our investiga-

TABLE 1. *Prevalence (%) of α1AT phenotypes in Saudi population.*

	Total no. investigated	α1AT phenotypes				
		MM	MS	MZ	SZ	ZZ
No. observed	204	177	19	5	2	1
No. expected[a]	203.56	175.1	19.5	8.3	0.46	0.20
Prevalence (%)	--	86.76	9.314	2.451	0.980	0.490

[a] Calculated using Hardy Weinburg equilibrium.

TABLE 2. *α1AT allele gene frequency in different populations.*

Population	Number investigated	α1AT allele gene frequency					Reference no.
		PiM	PiS	PiZ	PiF	PiI	
Spanish	378	0.8664	0.1124	0.0119	0.0026	0.0013	8
	810	0.875	0.116	0.007	–	–	14
	644	0.878	0.116	0.005	–	–	14
Indians	430	0.9942	–	0.0058	–	–	7
Italians	202	0.9501	0.0297	0.0099	0.0074	0.0025	15
	500	0.9110	0.0670	0.0150	0.0040	0.0020	12
Greeks	504	0.9600	0.0280	0.0020	0.0060	–	16
U.K.	4042	0.9303	0.0500	0.0141	0.0035	–	10
Finnish Laps	468	0.9957	0.0032	0.0010	–	–	17
Norwegian Laps	302	0.9917	–	0.0083	–	–	17
U.S.A. (whites)	904	0.956	0.023	0.014	0.003	0.003	18
French	1653	0.9019	0.0713	0.0142	0.0036	0.0036	9
Saudis	204	0.9265	0.0515	0.022	–	–	Present study

tion has also highlighted the need for further investigations of α1AT in a larger sample size to determine the presence of rare α1AT variants in the Saudi population.

Acknowledgment

This study was financially supported by a grant from RMSSS, King Saud University, Riyadh. We are also grateful to Miss Sakunda for technical assistance.

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OBESITY IN A PRIMARY HEALTH CARE CENTRE: A RETROSPECTIVE STUDY

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أجريت دراسة مراجعة على أطوال وأوزان ١٠٧٢ سعودياً (٤٧٧ رجلاً و٥٩٥ امرأةً) تتراوح أعمارهم بين ١٨ و٧٤ عاماً لتحديد انتشار السمنة بين السعوديين من المرضى الذين يراجعون مركز الرعاية الصحية الأولية بمستشفى الملك فهد الجامعي، بالخبر، في المنطقة الشرقية بالمملكة العربية السعودية. ومن إجمالي المجموعة اعتبرت نسبة ٥١,٥٪ من الرجال (حدود درجة الوثوق ٩٥٪ تتراوح بين ٤٦,٥ و٥٦,٠) يعانون من السمنة، ونسبة ٦٥,٤٪ من النساء (حدود درجة الوثوق ٩٥٪ تتراوح بين ٦١,٥ و٦٩,٢) يعانون من السمنة، عند اعتبار المعيار تجاوز منسب كتلة الجسم (الوزن مقسوما على مربع الطول) ٢٥ كغم / متر مربع. وكان عدد السمينات من النساء أكثر بدرجة هامة مقارنة بالرجال. لذا فمن الضروري إنشاء برنامج نشط للكشف عن السمنة وإجراء حملة مضادة للسمنة في المجتمع بحيث يشمل نصائح عن القوت وتعريف المرضى بالسمنة ومضاعفاتها.

In a retrospective study, the heights and weights of 1072 Saudis (477 men and 595 women), aged 18 to 74 years, were studied to determine the prevalence of obesity in Saudi patients attending the primary health care centre of King Fahd Hospital of the University, Al-Khobar, in the Eastern Province of Saudi Arabia. Of the total group, 51.5% (95% confidence interval, 46.5 to 56.0) of the men and 65.4% (95% confidence interval, 61.5 to 69.2) of the women were considered obese, using as the criterion a body mass index (wt/ht^2) of greater than 25 kg/m^2. Significantly more women were obese than men. An active detection program and campaign against obesity must be mounted in the community, and this should include advice on diet and the better education of patients with regard to obesity and its complications.

Obesity is not an uncommon finding, particularly in affluent societies [1,6], and it is the associated medical and social risks that especially make it a problem. Garrow [1] devised a chart for classifying obesity based on the body mass index (BMI), a concept that was first suggested over a hundred years ago by Quetelet, a Belgian mathematician [2]. Billewicz et al [3] compared various indices of adiposity and concluded that, while none was perfect, Quetelet's obesity index was reasonably satisfactory over a wide range of heights. Information on the prevalence of obesity in various countries [4] has been different mainly because there is no universally accepted index of obesity [5]. However, Garrow [1] estimated that, among adults in the U.K. and U.S. (using Quetelet's index), 25 to 33% have grade I obesity (BMI, 25 to < 30 kg/m^2), 4% have grade II obesity (BMI, 30 to 40 kg/m^2), and 0.05% have grade III obesity (BMI > 40 kg/m^2). Other studies [6], using 20% above desirable weight as an index of obesity, have estimated the prevalence rate for the U.S. population to be 24% for women and 14% for men, aged 18 to 74 years.

There are no known official data on the prevalence rate of obesity in the population at large in Saudi Arabia, though it is suspected to be high. The objective of this study was to estimate the percentage of women who are obese and to compare

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Accepted for publication 31 March 1990.

them with their male counterparts. Only Saudi men and women were studied. No attempt was made to examine socioeconomic factors, marital status, or parity.

Subjects and Methods

Patients seen at the primary health care centre of King Fahd Hospital of the University routinely have their heights and weights measured at the first visit. Only weight is recorded at subsequent visits. Weight was measured (with patients wearing light indoor clothing) in kilograms to the nearest 100 grams using a lever balance made by Seca (Germany) placed on a hard, level, uncarpeted floor. The instrument is recalibrated every six months. Height is measured with the patient standing upright with the entire foot planted on the platform. Measurements are made against a flat vertical surface using the fitted sliding headpiece of the lever balance and recorded to the nearest 0.5 cm.

The files of patients were retrospectively reviewed and only heights and weights recorded at the first registration were used. Only Saudi men and nonpregnant Saudi women between the ages of 18 and 74 years were included. Patients with either type of diabetes mellitus or diseases associated with fluid retention were excluded. The BMI of each patient was then calculated by dividing the weight (in kilograms) by the height (in meters squared).

Data were entered into the computer and analyzed using SPSS/PC+. The BMI for each subject was computed and prevalence rates of the various grades of obesity were estimated. Tests of hypothesis to determine the significance of the difference between the two sexes were carried out.

Obesity was subdivided into three grades in accordance with the Garrow classification [1]; mild (grade I), BMI 25 to < 30 kg/m^2; moderate (grade II), BMI 30 to 40 kg/m^2; and severe (grade III), BMI > 40 kg/m^2.

Results

The records of 1072 Saudis (477 men and 595 women) between the ages of 18 and 74 years were analyzed.

Table 1 shows the distribution of females and males according to their BMI. Of the total females, 206 (34.6%) were nonobese. Of those who were obese, 203 (34.1%) had grade I obesity, 166 (27.9%) had grade II obesity, and 20 (3.4%) had grade III obesity. Of the 477 men, 231 (48.4%) were nonobese, 167 (35%) had grade I obesity, 76 (15.9%) had grade II obesity, and only three (0.63%) had grade III obesity.

The between-sex differences in obesity rates are shown in Table 2. Severe obesity was significantly more prevalent in females as compared with males ($P = 0.001$). Although there was no significant difference in the prevalence rate of mild obesity ($P = 0.4$), the overall difference in the rates of all grades of obesity was significantly higher in women ($P < 0.0001$).

Detailed statistical studies of simple regression analysis of weight on age showed poor correlation for both sexes, ($r^2 = 0.03154$ for females, 0.04324 for males). Similarly, poor correlation was demonstrated between BMI and age for both sexes ($r^2 = 0.05386$ for females, 0.081892 for male).

TABLE 1. *Distribution of 595 women and 477 men aged 18–74 years, according to BMI.*

		Men		Women	
Obesity grade	BMI (kg/m2)	No. (%)	95% conf. interval	No. (%)	95% conf. interval
Nonobese	<25	231 (48.4)	42.0–54.8	206 (34.6)	28.1–41.1
Obese					
I (mild)	25–29.9	167 (35.0)	27.8–42.2	203 (34.1)	27.6–40.6
II (moderate)	30–40	76 (15.9)	7.7–24.1	166 (27.9)	21.1–34.7
III (severe)	>40	3 (0.6)	0–9.6	20 (3.4)	0–7.5
Subtotal		246 (51.5)		389 (65.4)	
Total		477		595	

BMI = body mass index.

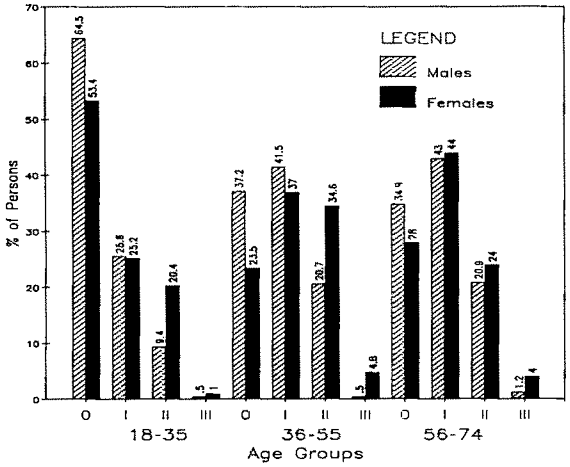

FIGURE 1. Frequency distribution of BMI according to sex and age group.

TABLE 2. *Test of significance in obesity rates between men and women aged 18–74 years.*

BMI, kg/m²	Proportion of obese Men (N = 477)	 Women (N = 595)	 *P*
Grade I	0.35	0.34	0.38
Grade II	0.16	0.28	< 0.0001
Grade III	0.006	0.034	0.001
Grades I+II+III	0.52	0.65	< 0.0001
Grades II+III	0.17	0.31	< 0.0001

BMI = body mass index.

Table 3 and Figure 1 show a comparison of distribution of males and females according to BMI and subdivided by the arbitrary age groups 18–35 yr, 36–55 yr, and 56–74 yr. In all age groups, more women were moderately or severely obese. However, an equal proportion of men and women were mildly obese in age groups 18 to 35 and there was a slight male preponderance in the 36 to 55 year age group. Subjects in age group 36 to 55 years were significantly more obese than those in age group 18 to 35 years (Table 4), and women predominated in both age groups ($P < 0.0006$).

Discussion

Although mild obesity (grade I) is not considered to pose an appreciable risk [1], marked obesity (grades II and III) is associated with increased morbidity and mortality [7]. Therefore it is important to determine its prevalence in a society so that proper preventive measures can be instituted, if findings indicate a serious problem.

In the present study, marked obesity was found in 16.5% of the men and 31.26% of the women. Overall, marked obesity was found in 24.72% of this adult population. This is considerably higher than the percentage cited by Garrow [1], who

TABLE 3. *Comparison of distribution of men and women according to BMI and age groups.*

Sex	Age groups	Body mass index (kg/m²) < 25	 25–29.9	 30–40	 > 40
Men (N = 477)	18–35	131 (64.5)	52 (25.6)	19 (9.4)	1 (0.5)
	36–55	70 (37.2)	78 (41.5)	39 (20.7)	1 (0.53)
	56–74	30 (34.9)	48 (43.0)	18 (20.9)	1 (1.12)
Women (N = 595)	18–35	110 (53.4)	52 (25.2)	42 (20.4)	2 (0.97)
	36–55	68 (23.5)	107 (37.0)	100 (34.6)	14 (4.8)
	56–74	28 (28)	44 (44)	24 (24)	4 (4)

Figures in parentheses are percentages.

TABLE 4. *Test of significance in obesity rates by age groups and gender.*

Sex	Age 18–35 yr No. of subjects	 BMI > 30 kg/m²	Age 36–55 yr No. of subjects	 BMI > 30 kg/m²	*P* value[a]
Males	203	20	188	40	0.001
Females	206	44	289	114	< 0.0001
P value[b]	–	< 0.001	–	< 0.0001	

[a] *P* value for difference in obesity rates between different age groups of the same gender.
[b] *P* value for difference between males and females of the same age groups.
BMI = body mass index.

found marked obesity in only 4.05% of adults of both sexes in the U.K. and U.S. The reasons for these differences are uncertain, but may be related to differences in dietary and sociocultural habits and the environment. The hot climate, especially in the summer, tends to discourage even the more ambitious from engaging in more physically demanding recreation.

Using a BMI > 30 kg/m^2 as the criterion for obesity in 467 nonpregnant Saudi women aged 15 to 49 years, Khwaja et al [8] observed an overall prevalence rate of 27% which was not statistically different ($P = 0.2$) from the 29.7% (95% confidence interval, 21.4–38.0) observed in our study which used similar criteria. However, they found that obesity was significantly related to age, and this was not the case in our study. The significant difference in prevalence for adult women and men cannot be accounted for by a difference in age, as both subpopulations had a similar mean age. This sex-related difference has also been observed in the Ten State Nutrition Survey [9]. The reasons are uncertain, but the difference may reflect different eating patterns or hormonal secretions. The obesity rate in a population increases considerably at about 40 years of age [10]. In our study population, obesity was uncommon in the relatively younger age groups. In our environment, and particularly in urban areas, women tend to lead a predominantly sedentary life, thus increasing the likelihood of obesity. Women do not have as much active outdoor life as men.

Attitudes toward obesity vary with culture. A community-based study conducted by one of the authors (TB) revealed that women who were visibly obese did not consider themselves so. This sociocultural attitude was also suggested by Dawson [11], who analyzed the ethnic differences in overweight females using data from the 1985 National Health Interview Survey and who remarked that "women's perceptions of whether or not they are overweight are more strongly influenced by their weight relative to their peers than by their weight relative to an arbitrary, health-based standard."

In the present population, mild and moderate obesity were common. Our results are not necessarily representative of other areas in the Kingdom and thus further studies are needed to delineate the extent of obesity on a national level. Our results, however, do suggest that obesity is a major problem for the family doctor and the primary health care team who must be actively involved in its prevention. In view of the polygenic origin [12] of obesity, it is important in constructing treatment programs for the obese that factors such as sociocultural background be considered. The primary health care teams are ideally suited for detecting and preventing obesity.

Acknowledgments

Our sincere thanks to Dr. Samir H. Abdul-Jauwad, PhD, for his invaluable assistance in the computer analysis of the data.

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ETIOLOGY AND CLINICAL PATTERN OF FULMINANT HEPATITIS IN IRAQ

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أجريت دراسة استطلاعية على ٢٥٣ حالة لالتهاب الكبد الحُموي الحاد، منها سبع وأربعون حالة من النوع الخاطف (١٨,٦٪). شملت الدراسة خمسة عشر رجلاً واثنان وثلاثين امرأة. تراوحت أعمارهم من السابعة إلى الستين (متوسط العمر ٢٨ عاما). ظهر الدليل المصلي لالتهاب الكبد الحُموي الحاد نوع (أ) في حالة واحدة (٢٪)، والتهاب الكبد الحُموي الحاد نوع (ب) في ١٣ حالة (٢٨٪)، والتهاب الكبد الحُموي الحاد نوع (د) في حالة واحدة (٢٪)، والتهاب الكبد الحُموي الحاد سوى (أ) و(ب) في ٣٢ حالة (٦٨٪). تبين وجود التهاب الكبد الخاطف في نسبة ٢,٦٪ من حالات التهاب الكبد الحُموي الحاد نوع (أ)، وفي نسبة ١٦,٢٥٪ من حالات التهاب الكبد الحُموي الحاد نوع (ب)، وفي حالة واحدة من حالتي التهاب الكبد الحُموي الحاد نوع (د) شديد الالتهاب، وفي نسبة ٢٤,٨٪ من حالات التهاب الكبد الحُموي الحاد سوى (أ) و(ب). أظهرت الصورة السريرية في النوعين الرئيسيين وهما التهاب الكبد الحُموي الحاد نوع (ب) والتهاب الكبد الحُموي الحاد سوى (أ) و(ب)، تميز الأخير بطول السيرة السريرية وشدتها وبارتفاع معدل الوفيات (P<0.001) . ويوضح أيضا ارتفاع معدل الوفيات بين الإناث في عمر الحمل مقارنة بالذكور من فئة العمر نفسها (P<0.001) .

Of 253 prospectively studied cases of acute viral hepatitis (AVH), 47 were fulminant (18.6%). There were 15 males and 32 females. Their age ranged from 7 to 60 years (mean, 28 years). Serological evidence of AVH-A was found in one case (2%), AVH-B in 13 cases (28%), AVH-D in one case (2%), and AVH-NANB in 32 cases (68%). Fulminant hepatitis was found in 2.6% of AVH-A cases, in 16.25% of AVH-B cases, in one of two AVH-D superinfections, and in 24.8% of the AVH-non-A, non-B (NANB) cases. The clinical picture in the two main etiological categories, namely the AVH-B and the AVH-NANB, showed that the latter possessed a more prolonged and severe clinical course with higher mortality (*P* < 0.001). It also showed a higher mortality in females of the child bearing age, compared with males of the same age group (*P* < 0.001).

The availability of highly specific tests for accurately diagnosing the different viruses that cause hepatitis has made it possible to differentiate fulminant hepatitis due to viruses A, B, D, and non-A, non-B (NANB). It has also helped in the study of the differences in the clinical picture among these different etiological categories, especially in relation to presentation, pregnancy, and prognosis. There have been few reports on this subject in general [1–4] and none from Iraq.

Patients and Methods

Of 253 prospectively studied patients with acute viral hepatitis (AVH) consecutively admitted to Ibn El-Khateeb Infectious Diseases Hospital, Baghdad, during one year (1984–1985), fulminant hepatitis occurred in 47 patients.

The diagnosis of AVH was made on the basis of

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Accepted for publication 2 April 1990.

characteristic symptoms, signs, and laboratory investigations (aminotransferase activity double the normal and elevated serum bilirubin of the direct type) and exclusion of other causes of jaundice. Diagnosis of fulminant hepatitis was made when signs of encephalopathy developed within eight weeks of the onset of illness [5]. All grades of encephalopathy were included; its onset and progression from grade I to IV or to recovery was recorded in each case, then studied according to the different etiological categories. None of the patients was treated in a specialized liver intensive care unit.

AVH-A was diagnosed by the presence of anti-hepatitis A virus IgM in the serum, AVH-B by the presence of high titers of anti-HBc IgM with or without HBsAg positivity. AVH-D superinfection was diagnosed in patients positive for HBsAg, negative for anti-HBc-IgM, and positive for delta antigen and/or anti-delta IgM. Those cases that presented late in the disease and were positive for anti-delta IgG only were also considered as cases of delta superinfection. Patients with high titers of anti-HBc IgM, with or without HBsAg, were considered to have hepatitis delta coinfection if the delta antigen and/or anti-delta IgM were also positive. Patients negative for all parameters were tested for antibodies against cytomegalovirus (CMV), Epstein-Barr virus (EBV), and herpes simplex virus (HSV). Those cases negative for all parameters were considered to result from infection with one of the NANB viruses. Hepatitis A and B markers were determined with enzyme-linked immunosorbent assays (ELISA), using commercially available kits from Abbot (Havab M, Auzyme, Corzyme-M). The delta virus markers were sought using experimental kits from Organon Teknika (Hepanostika). CMV and HSV infections were diagnosed by looking for IgM antibodies with ELISA tests obtained from Behring (Enpygnost-CMV and HSV). EBV infection was detected using IgG anti-VCA with an indirect immunofluorescence assay from Gull.

F tests and chi-square tests were used to determine statistical significance.

Results

Of the 253 cases of AVH studied, 47 were fulminant (18.5%). There were 15 males and 32 females, with an age range of 7 to 60 years (mean, 28 years).

TABLE 1. *Clinical and laboratory findings in fulminant hepatitis due to HBV and NANB.*

Clinical and laboratory findings	HBV	Non A Non B
Mean age (yr)	27.6	28.7
Age range (yr)	9–6	7–48
Male:female	2:11	24:33
Case fatality rate	30.5	72.7
Mean serum bilirubin (μmol/L)	419	530
Mean alanine transaminase (μkat/L)	8.64	7.33
Prolongation of prothrombin (sec)	19	29
Mean interval between onset of symptoms and onset of encephalopathy (days)	19	29

HBV = hepatitis B virus; NANA = non A non B.

Serological evidence of AVH-A infection was found in one case only (2%), AVH-B infection in 13 cases (28%), AVH-D infection in one case (2%), and AVH-NANB viruses in 32 cases (68%). Studying the occurrence of fulminant hepatitis in relation to the different viral etiological categories, we found that fulminant hepatitis occurred in 2.6% of the AVH-A cases, in 16.25% of the AVH-B cases, in 24.8% of the AVH-NANB cases, and in one of the two cases of AVH-D superinfection. The one case of AVH-A was a 9-year-old boy who was known to be G6PD deficient. He had severe hemolysis in addition to AVH and developed grade III encephalopathy, from which he recovered after supportive therapy. The one case of AVH-D superinfection was in a 25-year-old male, seen seven weeks after the onset of symptoms with grade IV encephalopathy, and who died soon after. Analysis of the two main groups of fulminant hepatitis, namely B and NANB, showed that NANB had a more severe course and higher mortality ($P < 0.05$) (Table 1). Comparing the occurrence and severity of B and NANB infection in females of the childbearing age (pregnant and nonpregnant) with males in the same age group (15–50 years), the case fatality rate (CFR) was significantly higher in females ($P < 0.001$). There was also a significantly higher CFR in nonpregnant women compared with pregnant women ($P < 0.01$) (Table 2).

The vast majority of fulminant cases of hepatitis were between 15 and 50 years of age (Table 3).

TABLE 2. *Age and CFR in FH-B and FH-NANB according to sex and pregnancy.*

	FH-B				FH-NANB			
Patients	No.	Mean age (yr)	Age range (yr)	CFR (%)	No.	Mean age (yr)	Age range (yr)	CFR (%)
Pregnant women	1 (4%)	25	–	0	6 (25%)	30	20–35	83
Nonpregnant women	9 (10%)	27	18–33	83	15 (17%)	31	18–41	86
Males	1 (1.3%)	50	–	0	9 (12%)	28	15–38	56

FH = fulminant hepatitis; CFR = case fatality rate; NANB = non A non B.

TABLE 3. *Age distribution of FH cases according to age.*

Patients	< 15 yr	15–50 yr	> 50 yr
Females	4	31	1
Males	1	10	0
Total	5	41	1

Discussion

The most common cause of fulminant hepatitis in this series were the NANB viruses (68%), followed by the B virus (28%). This finding is unusual in view of the fact that Iraq is moderately endemic for the B virus [6]. Papaevangelou et al [2] found the B virus was responsible for 73.9% of the cases of fulminant hepatitis in Greece, a country with similar endemicity to Iraq for HBV. The preponderance of NANB as a cause of fulminant hepatitis in Iraq seems to indicate concomitant endemicity of one or more types of NANB viruses. It may also be partially related to our finding that the fulminant form occurred most frequently among the NANB-AVH cases. A similar preponderance has been reported from many Western countries [1,3,4].

The rarity of the delta virus infection as a cause of fulminant hepatitis in this study is interesting because many countries in the Middle East, including Iraq, have been shown to have a high prevalence of delta infection in asymptomatic carriers and patients with chronic liver diseases [7]. Reports from other countries have incriminated the delta virus in the etiology of fulminant hepatitis [8,9]. This discrepancy may be explained by the varying degree of endemicity of the delta virus. Countries with high endemicity would have a greater subclinical infection than those countries where the virus has recently been introduced [10,11].

The differences in the clinical course and prognosis between the NANB and B groups are similar to those reported by Gimson et al [1]. These authors showed a longer interval between the onset of symptoms and the onset of encephalopathy, suggesting that the process underlying the liver damage in fulminant hepatitis NANB appears to be a slower process compared with that in the B group. Although the same finding was observed in our series, the difference was not statistically significant ($P > 0.05$). The significantly higher mortality in the NANB group compared with the B group ($P < 0.001$) indicates a more aggressive interaction between the pathogenic agent and the liver. Whether this is due to a direct cytopathic action of the virus or to an immunological insult awaits the identification of the different viruses involved.

The significantly higher CFR in nonpregnant compared with pregant women ($P < 0.01$), and in women regardless of pregnancy compared with males of the same age group ($P < 0.001$), is an important finding (Table 2). Several authors working in the Middle East and India reported a worse prognosis for pregnant women with hepatitis [12–14] in contrast to the experience in western Europe [15,16]. We have reported a higher mortality in Iraqi females of childbearing age [17] and our results suggested that it is the female sex and not pregnancy that is responsible for the higher mortality in females of this age group. However, larger series should be studied to clarify this point. When tests become available for the diagnosis of the different NANB viruses, the controversy may be solved.

Acknowledgment

We thank Daib A. Aziz, PhD, Assistant Professor, College of Agriculture, University of Baghdad, for his valuable help in performing the statistical analysis.

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TRENDS IN PEDIATRIC CASUALTIES IN A REGIONAL HOSPITAL OF KUWAIT

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كان الغرض من هذه الدراسة هو التحليل الإحصائي لخدمات رعاية الطوارىء في قسم الأطفال في مستشفى الفروانية بالكويت. ابتدأت الدراسة في ١ يوليو/ تموز ١٩٨٧م، وانتهت في ٣٠ يونيو/ حزيران ١٩٨٨م، سُجل خلالها ما مجموعه ٧٧,٤٩٧ حالة (٤١,٥٩٤ [٥٣,٧٪] ذكور، و٣٥,٩٠٣ [٤٦,٣٪] إناث). شكل الأطفال الكويتيون ٤٠,٧٣٨ (٥٢,٥٪) من المجموع. وشكل الأطفال من سن ٢ إلى ٥ سنوات ٢٢,٨٠٥ (٢٩,٤٪) من الحالات، في حين شكلت فئة الأعمار من شهر واحد إلى سنة واحدة ثاني أكبر مجموعة من الحالات (١٥,٤٧٥، [١٩,٩٪]). كان أعلى معدل للدخول إلى المستشفى في شهر فبراير/ شباط (٨,٤٢٥ [١٠,٨٪])، وكان يوم الجمعة هو أكثر الأيام ازدحاماً (١٣,٥٦١ [١٧,٥٪]). كان هناك ٦١,٢٤٢ (٧٩,٠٢٪) إحالة ذاتية. كانت الأمراض التنفسية هي أكثر الأسباب تواردا في قسم الطوارىء، إذ بلغ مجموعها ٥١,٥٨٣ (٦٦,٥٪)، تلاها حالات الالتهاب المعدي المعوي (١٩,٨٩٨ [٢٥,٧٪]). تشير هذه الدراسة إلى زيادة خطيرة في عدد المراجعين لعيادات الطوارىء في مستشفى الفروانية. وإذا ما استمرت هذه الزيادة فإنها لن تزيد من أعباء الهيئة الطبية/ التمريضية فحسب، بل إنها ستؤثر سلباً على الجودة النوعية للخدمات المقدمة.

The purpose of this study was to statistically analyze the emergency care services of the Paediatric Department of Farwania Hospital, Kuwait. The study was conducted from 1 July 1987 until 30 June 1988, during which a total of 77,497 cases were recorded (41,594 [53.7%] males; 35,903 [46.3%] females). Kuwaiti children represented 40,738 (52.5%) of the total. Children aged 2 to 5 years constituted 22,805 (29.4%) of the cases, and the age group 1 month to 1 year comprised the second largest group (15,475; 19.9%). Admissions peaked in February (8,425 [10.8%]) and Friday was the busiest day (13,561 [17.5%]). There were 61,242 (79.02%) self-referrals. Respiratory diseases were the most common reason for emergency room visits, and totaled 51,583 (66.5%), followed by gastroenteritis with 19,898 (25.7%). This study points up an alarming increase in the number of visits to the casualty clinics of Farwania Hospital. If this increase continues, this will not only markedly increase the burden to staff but will also adversely affect the quality of services.

Over the past few years, there has been an increase in the number of patients attending the casualty clinic of the Paediatric Department of Farwania Regional Hospital. A high percentage of these patients have required primary care and not emergency medicine, a finding reported by other centers [1–7]. A lack of information regarding the users of emergency departments in England was stressed by the Korner Working Party [8] and a similar lack exists for Kuwait.

This study aims at a statistical analysis of emergency services, and the following parameters were considered: the number of attenders, types of illness, peak hours of use, and the possible misuse of the pediatric casualty services. To the best

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Accepted for publication 16 April 1990.

of our knowledge, no similar study has been done in Kuwait.

Methods

Farwania Hospital is a regional hospital serving a total population of 426,319. Its bed capacity is 520, of which 150 beds are allocated for pediatric use. There are local referring polyclinics that provide complete primary medical care from 7:30 AM until midnight. The policy of the hospital is to examine all patients, with or without referral. Five physicians staff the casualty services around the clock.

The present study was conducted 1 July 1987 to 30 June 1988. The information obtained for all patients consisted of: age, sex, nationality, day of week and hour of attendance, referral versus nonreferral, casualty diagnosis, diagnostic tests, and whether the patient was admitted.

Results

A total of 77,497 cases were recorded, and consisted of 41,594 (53.6%) males and 35,903 (46.4%) females (male to female ratio, 1.16:1). The males outnumbered the females in all age groups. Kuwaiti children represented 40,738 (52.5%) and children of all other nationalities constituted 36,759 (47.5%).

Figure 1 shows the age distribution. There were 22,805 (29.4%) children (aged 2–6 years), and these represented the largest group of patients, followed by the age group 1 month to 1 year (15,475 [19.9%]). Figure 2 illustrates the pattern of the total number of attenders and the total number of admissions throughout the year.

February attendance was the highest at 8425 (10.8%), while July was the lowest with a total attendance of 4308 (5.5%). In general, the winter months (October through May) were the busiest. However, the number of hospital admissions was almost the same throughout all months of the year, with a total of 7246 (9.35%).

Friday was the busiest day throughout the year (17.5%), followed by Thursday (14.7%) and Saturday (13.5%) (Figure 3). The busiest time of day was from 8:00 PM to 3:00 AM, representing 56.22% of the total attendance per 24 hours. Conversely, the least busy period was from 3:00 to 7:00 AM (4.77%) followed by 7:00 AM to 1:00 PM (18.27%) (Figure 4).

The number of nonreferred cases was 61,242 (79.02%) (Figure 5). Figure 6 shows the pattern of

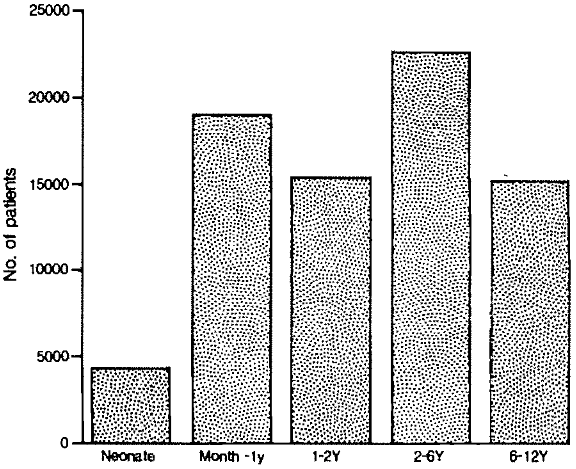

FIGURE 1. Age distribution of patients attending the pediatric casualty clinic during July 1987 to June 1988.

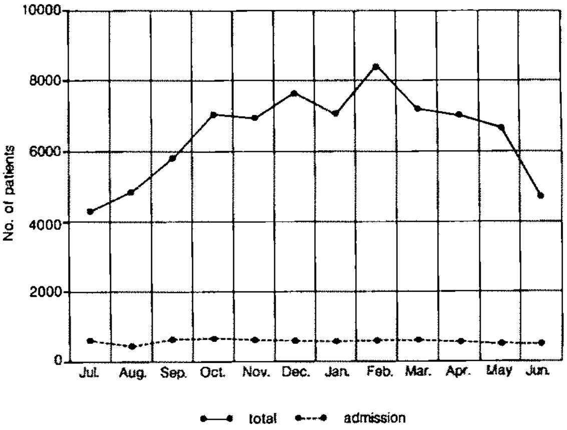

FIGURE 2. Admissions and total number of patients during July 1987 to June 1988.

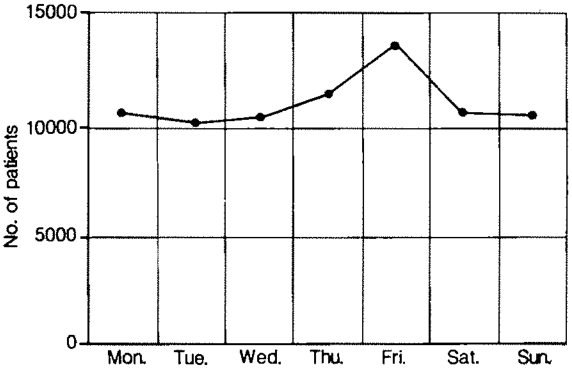

FIGURE 3. Daily trends in the pediatric casualty clinic July 1987 to June 1988.

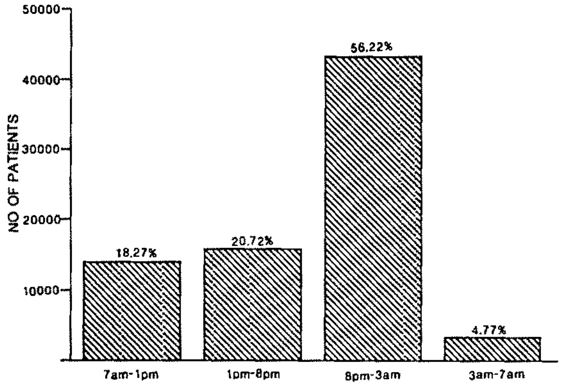

FIGURE 4. Round-the-clock trends in the pediatric casualty clinic during July 1987 to June 1988.

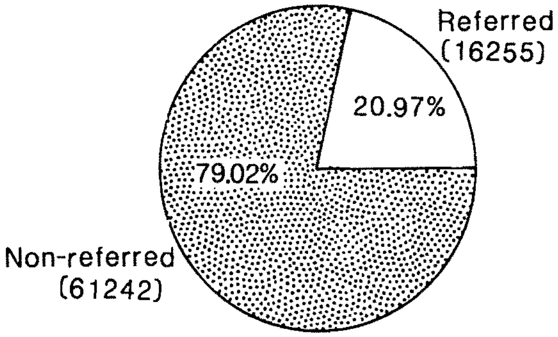

FIGURE 5. Comparison of referred to nonreferred patients in the pediatric casualty clinic during July 1987 to June 1988.

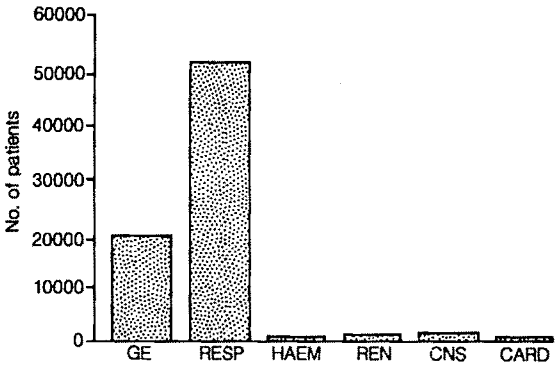

FIGURE 6. Pattern of diagnosed diseases among attenders to the pediatric casualty clinic during July 1987 to June 1988. (*GE* = gastroenteritis; *RESP* = respiratory; *REN* = renal; *CNS* = central nervous system; *CARD* = cardiac.)

diagnosed diseases that prompted visits to the emergency room. Respiratory diseases were the most common (51,583; 66.5%) followed by gastroenteritis (19,898; 27.5%).

Mild cases of simple upper respiratory tract infections and cases of simple gastroenteritis with no dehydration that could be managed in the clinics without hospitalization accounted for 32,083 (41.4%) and 8757 (11.3%), of the cases respectively. These cases account for 40,840 (52.7%) of the total attendance. During the year 1985 to 1987, the number of visits to the pediatric casualty service were 45,978, 59,619, and 70,200 patients, respectively.

Discussion

The results of this study clearly demonstrate the abuse of casualty services offered by pediatric department of Farwania Regional Hospital, which ultimately is reflected in the quality of the services. We now handle simple routine walk-in cases totaling 40,840 (52.7%) patients. This number has progressively increased and represents 1.68 times the number of cases seen 3 years ago. Most of these patients needed primary care rather than casualty assistance.

The pediatric emergency facilities were frequently used for nonurgent problems by parents who found them convenient sources of health care for their children, an observation made by others [7,10–13].

The male cases (53.6%) outnumbered the female (46.4%), as has been observed in other studies [14,15]. Children less than 1 year of age constituted 30.6%, which agrees with other reported figures [16,17]. Self-referral cases formed 79.02% of the total attendance, in agreement with observations of others [18,19]. The busiest months were the winter months (October to May), with February the peak month. The busiest day was Friday, which is the second day of the weekend in Kuwait. This is also similar to findings in Western countries where Saturdays have proved to be the busiest day [2,8,14]. The busiest period of the day was from 8:00 PM to 3:00 AM; other workers have reported 8:00 AM to mid-day as the busiest time [8,14].

Respiratory illnesses (66.5%) were the most common presenting complaints in our study, and our count is higher than that reported by others [3,14,20]. This is probably due to increased viral infections during the busy winter months of the year. The total number of admissions was 9.3%, a figure similar to that reported by others [10]. Conversely, figures as high as 24.5% have been reported by some workers [14]. The evenly distributed number of admissions throughout the year could be explained by the increased abuse of the casualty services during the winter months.

Although primary health care centers in the Farwania area are well established, distributed, and equipped for serving the pediatric age group, the number of nonreferral children attending the pediatric casualty is increasing, in contrast to the observation of Hochheiser et al [3]. This may be attributed to parents' belief that the primary health care system does not provide their children with as good a standard of care as that available in the hospital. Similar findings have been reported by others [10–13]. Moreover, the Ministry of Public Health's policy of examining any patient coming to the hospital, with or without referral, and allowing walk-in patients freely after midnight increases the attendance in the casualty clinic.

To reduce the number of visits to the pediatric casualty clinic, we recommend the following: (1) improving the standard of services at the polyclinics; (2) limiting the services to patients who cannot be managed in the clinics; (3) increasing the patient–doctor relationship by using mass media to inform and educate the public regarding the facilities and the services available in the clinics; and (4) limiting medications available in the pediatric casualty clinic to those also available in the clinic.

If the attendance at the casualty clinics continues in this vein, it will markedly increase the burden on the clinic staff and adversely affect the quality of the services.

Acknowledgment

We are grateful to Dr. A. Al-Teebi for his kind revision and constructive criticism of the manuscript. Also, we are grateful to Dr. Moosa Al-Juwaiser and Ms. Aida B. Adomian for their kind help in preparing the manucript.

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GASTRIC TORSION: NOT SUCH A RARE ENTITY

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تتضمن المقالة وصفاً لسبعة مرضى عانوا من انفتال معدي مزمن وشوهدوا خلال فترة زمنية طولها ٢٨ شهرًا. كان أربعة منهم أطفالاً، بينهم ثلاثة رُضع. كان الرُضع يعانون من القُياء القذفي واثنا منهم كانا يعانيان أيضاً من تخلّف في النمو. أما المرضى البالغون فكانوا يعانون من ألم شرسوفي وقُياء. وأكدت الصور الشعاعية المتسلسلة لأعلى القناة الهضمية صحة التشخيص في كل الحالات. وقد يحدث أحياناً أن لا يتبه إلى المظهر الشعاعي التقليدي لمعدة تقع معترضة عبر الشرسوف، بينما يقع الفؤاد والقعر في وضع أدنى من جسم المعدة وبوابها، وتناقش المقالة الخيار الجراحي للعلاج. لم نجد شذوذاً مرافقاً في أربع من الحالات الست التي أجريت لها عمليات جراحية. لكن رضيعاً واحداً كان مصاباً برتق المعي، وتشوهات وعائية، وفتق سرّي، والتهاب صفاقي عقي سابق. وكان رضيع ثان يعاني من انغلاف صائمي ـ صائمي. إن من المفيد التزام نسبة عالية من الشك في المرضى الذين يتقدمون بشكوى من ألم بطني معاود أو في الرُضع الذين يعانون من قُياء لا تفسير له أو من تخلّف في النمو. كما يستحسن إجراء التصوير الشعاعي المتسلسل للجزء العلوي من القناة الهضمية للبالغين أثناء معاناتهم من الألم.

We describe seven patients who suffered chronic gastric torsion, seen during a 28-month period. Four were children, of which three were infants. The infants had projectile vomiting and two also had failure to thrive. The adults presented with epigastric pain and vomiting. Upper gastrointestinal series clinched the diagnosis in all patients. The classic radiographic presentation of a stomach lying across the epigastrium with the cardia and fundus in a dependent position to the body of the stomach and pylorus may be overlooked in some cases. Choice of surgical procedure in its management has been discussed. There was no associated abnormality in four of the six operated cases. One infant had an atretic bowel, vascular anomalies, umbilical hernia, and previous meconium peritonitis; a second infant had jejunojejunal intussusception. A high index of suspicion is warranted in patients presenting with recurrent abdominal pain or in infants with unexplained vomiting and failure to thrive. Upper gastrointestinal series in adults should preferably be performed while the pain is present.

Gastric torsion, otherwise known as gastric volvulus, is a very rare abnormality. Youssef et al [1], in a review of their experience over a 30-year period, encountered only 10 cases. In their search of the literature up to 1980, they found 300 cases, of which only 50 presented in children. Gastric torsion can present either acutely or chronically. In the acute presentation, gastric torsion could result in gastric hemorrhage [2], gastric ischemia, and infarction [3]. Most cases present in the chronic form, and such patients suffer from recurrent epigastric pain and vomiting with resultant multiple hospital admissions. The clinical presentation is nonspecific and an upper gastrointestinal (UGI) series is the definitive examination in making the diagnosis. Unfortunately, the radiographic presentation may be overlooked or absent if the examination is done when the patient is not in pain.

The purpose of this communication is to describe seven cases of gastric torsion seen by us over a 28-month period between July 1987 and

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Accepted for publication l6 April 1990.

TABLE 1. *Summary of seven patients with gastric torsion.*

Patient no.	Age	Sex	Presenting features	Radiological findings	Surgical treatment	Remarks
1	4 mo	F	Persistent projectile vomiting. Postneonatal surgery for meconium peritonitis.	Organoaxial torsion of the stomach; overlooked on a previous UGI series.	Gastric fixation + stricturectomy + repair of umbilical hernia.	Operated at age 21 days for intestinal obstruction; meconium cyst, meconium peritonitis, small bowel narrowing, vascular anomalies; baby has settled 1 year after gastropexy.
2	40 da	M	Nonbilious projectile vomiting almost after every feed + failure to thrive.	Organoaxial torsion of the stomach.	Gastropexy done.	Baby settled.
3	6 yr	M	Recurrent abdominal pain with vomiting and many hospitalizations.	Organoaxial torsion on UGI study during an episode of pain.	Gastropexy done.	One episode of postop pain; now settled.
4	61 yr	M	Heartburns, vague aches and pain, previously diagnosed as irritable bowel syndrome with hiatus hernia.	Hiatus hernia (sliding), organoaxial torsion.	Unknown.	Referred for UGI from outside hospital.
5	25 yr	M	Recurrent epigastric pain with vomiting.	Organoaxial torsion of the stomach.	Nissen's fundoplication and gastropexy done.	Mentally retarded; gastritis on endoscopy.
6	27 yr	M	Recurrent epigastric pain with vomiting relieved by pressure on epigastrium.	Organoaxial torsion of the stomach.	Nissen's fundoplication.	Normal endoscopy; all other lab tests normal.
7	5 mo	F	Failure to thrive, not retaining feeds, right flank mass.	Organoaxial torsion and reflux, mid small bowel obstruction.	Reduction of jejunojejunal intussusception, gastrostomy.	Short follow up.

UGI = upper gastrointestinal.

November 1989 at the Asir Central Hospital in the Kingdom of Saudi Arabia. Our observations suggest that this entity may not be rare in this part of the world.

Material and Comment

Between July 1987 and November 1989, seven cases of gastric torsion were diagnosed by UGI series at the Asir Central Hospital in the Kingdom of Saudi Arabia (Table 1). Four patients were children (aged, 40 days, 4 months, 5 months, and 6 years) and three were adults. There were five males and two females. The typical clinical presentation consisted of recurrent epigastric pain and vomiting. In the three infants, persistent projectile vomiting was the common feature and this was associated with failure to thrive in two infants. The adults had had recurrent episodes of epigastric pain, and this had led to multiple hospitalizations and investigations. One of our patients (No. 5) was known to have swallowed multiple foreign bodies, and psychiatric care was recommended during one of his many hospitalizations. In one patient the abdominal pain was not usually relieved by anything but pressure on the epigastrium. Physical examination revealed only epigastric tenderness in the adults, and laboratory findings were usually normal. Endoscopy was not helpful in the two patients in whom it was performed.

In all seven cases, the UGI series showed the classic signs of organoaxial torsion (Figure 1). These signs include a stomach lying across the epigastrium with the cardia and gastric fundus in a dependent position to the body of the stomach, while the greater curvature is superior to the lesser

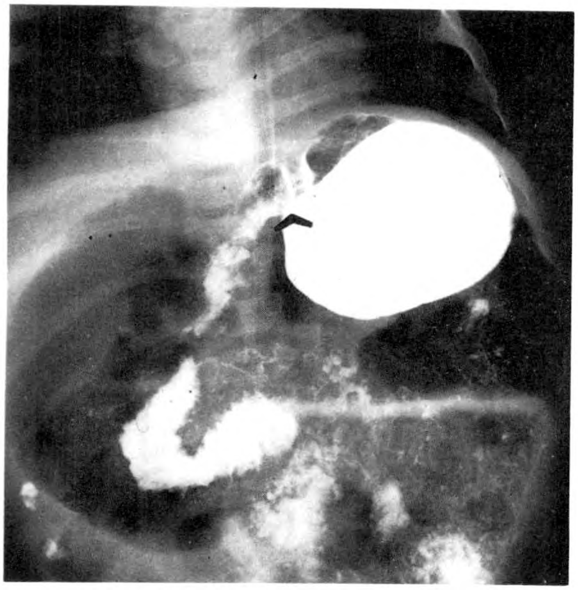

FIGURE 1. View of upper gastrointestinal series in a 4-month-old infant, showing the classic picture of gastric torsion. Observe the cardia *(black arrow)* in a dependent position to the pylorus and duodenai cap, which is directed inferiorly.

curvature and the antrum and duodenal bulb are vertically directed. Double fluid levels may be seen in the stomach when the patient is in the lateral erect position.

In patients 3 and 6, the initial films were normal and it was in the process of turning the patients on the table that the classic picture emerged. Three of the patients had had previous UGI series, which were considered normal. A previous study was available and when it was reviewed the lesion was apparent but had been initially overlooked.

Anterior gastropexy was prescribed for five of the six patients who underwent operation. In four patients this involved securing the anterior wall of the stomach to the anterior abdominal wall by interrupted silk sutures; one of these four patients had an additional Nissen's fundoplication. The fifth patient, an infant, underwent gastrostomy, both for fixation and feeding purposes. During one year of follow-up in three patients there was no recurrence of the torsion.

Discussion

Gastric torsion in the chronic form results in significant morbidity, and is more common in adults than in children. An index of suspicion is therefore required in patients presenting with recurrent epigastric pain, as this nonspecific symptom may exist in other diseases. In children, vomiting regurgitation and epigastric pain should alert the treating physician to the possibility of gastric torsion. It should be suspected in the infant who is not retaining feeds or is failing to thrive, once the usual causes are excluded.

Several underlying abnormalities may predispose to torsion, including diaphragmatic defects, hiatus hernia [3–5], asplenic syndrome [6], defective development of the left lobe of the liver [7], and absence of the gastrosplenic ligament [8]. About one-third of the patients have no associated abnormality. Four of our seven patients had no associated abnormalities. A retrocardiac double fluid level seen on a chest x-ray study in a suspected case of hiatal hernia should raise the question of intrathoracic gastric torsion [3]. The familial occurrence of gastric torsion has also been reported [9]. An intrathoracic location is fairly common, though all of our seven cases were intraabdominal and were of the organoaxial type.

Complications include gastric ischemia [3,6], respiratory distress in babies [8], and gastric hemorrhage [2], particularly in the acute form. Extrahepatic biliary obstruction has also been reported [4]. The diagnosis should be suspected in the context of these life-threatening complications. We did not encounter any notable complications, possibly because all our cases were chronic or recurrent. However, the chronic form can become acute. The UGI study is the most reliable diagnostic method. It should preferably be done when the patient is in pain because these torsions can spontaneously reduce, leading to a false negative diagnosis. The stomach may also present a normal appearance, but subsequent twisting of the body may reveal the abnormality, as was the case in some of our patients. Therefore some turning around should be done, and the usual recumbent and erect films are mandatory. The classic radiológical changes can also be overlooked. The lesion may also reduce spontaneously during the examination.

There is no known effective conservative treatment for gastric torsion. The only definitive therapy is surgical. Most cases of gastric torsion are due to some underlying abnormalities resulting in deficient fixation of the stomach. Therefore fixation of the stomach is generally needed, along with repair of any associated abnormalities. Surgical treatment varies and can consist of anterior gastropexy [1,8], gastrojejunostomy [10], and gastrostomy [11]. The procedure of choice depends on the condition of the stomach, associated anomalies, and the condition of the patient at the time of presentation.

In conclusion, gastric torsion does not appear to be very rare in our environment. An index of suspicion should be maintained in patients who present with recurrent abdominal pain but whose laboratory examinations have been normal. A carefully done UGI series, particularly when the patient is in pain, which includes turning the patient around several times, may yield a fruitful result and enable timely surgical treatment.

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MANAGEMENT OF SYMPTOMATIC PATENT DUCTUS ARTERIOSUS IN VERY LOW-BIRTH-WEIGHT INFANTS

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أجريت دراسة مراجعة لتسع وثلاثين (٣٩ رضيعاً، وُلدوا قبل تمام الأسبوع الثلاثين من الحمل، من أجل تحليل معدل وقوع القناة الشريانية السالكة ظاهرة الأعراض وتدبيرها والمراضة الناجمة عنها. ظهرت أعراض القناة الشريانية السالكة على واحد وعشرين رضيعاً (٥٣,٨٪) وأجري إغلاقها جراحياً لدى أحد عشر رضيعاً (٥٢,٣٪). تميز الرُضّع في هذه المجموعة بتدني وزن الولادة ومتلازمة ضائقة التنفس الشديدة ومراضة مرتفعة، مقارنة بالمجموعة التي تم تدبيرها طبياً. لم يعانِ الرُضّع الذين استجابوا للتدبير الدوائي من نسبة مراضة عالية مقارنة بالمجموعة الضابطة التي لم تصب بأعراض القناة الشريانية السالكة. لم تنجع المعالجة بعقار اندومثاسين لدى الرُضّع الذين كان وزن ولادتهم دون الثمانمائة غرام. تشير نتائجنا إلى أن نسبة المراضة العالية التي شوهدت لدى مجموعة القناة الشريانية السالكة قد تعود إلى متلازمة ضائقة التنفس والجراحة وتدني وزن الولادة عن ٨٠٠ غرام. ويشك في جدوى الاستخدام الوقائي لعقار الاندومثاسين لدى هذه المجموعة.

A retrospective study of 39 infants under 30 weeks' gestation was carried out to analyze the incidence, management, and morbidity resulting from symptomatic patent ductus arteriosus. Symptomatic patent ductus arteriosus developed in 21 (53.8%) infants. Eleven (52.3%) infants underwent surgical closure of the ductus. The infants in this group had lower birth weight and severe respiratory distress syndrome and higher morbidity, compared with the medically managed group. The infants who responded to medical management did not have higher morbidity compared with the control group who did not sustain symptomatic patent ductus arteriosus. Indomethacin treatment was not effective in infants with a birth weight less than 800 gm. Our findings indicate that the higher morbidity seen in the symptomatic patent ductus arteriosus group may be due to respiratory distress syndrome, surgery, and birth weight under 800 gm. Prophylactic use of indomethacin may have a doubtful value in this group.

Patent ductus arteriosus is a common clinical condition in very-low-birth-weight infants [1]. If the left-to-right shunt through the ductus becomes significant, this will worsen or give rise to symptoms of respiratory distress, and this condition is called symptomatic patent ductus arteriosus (SPDA). Patent ductus arteriosus has also been implicated in the etiopathogenesis of bronchopulmonary dysplasia (BPD), necrotizing enterocolitis, and intraventricular hemorrhage (IVH) in very-low-birth-weight infants [2–5]. Since the introduction of indomethacin in 1976 for the medical management of PDA and the advent of surgical closure of ductus arteriosus in very-low-birth-weight infants, the question of prophylaxis has arisen. Even though surgery has been performed in the neonatal intensive care units in certain centers, it is not usually the first choice in the management of infants with PDA [5,6]. However, the response to indomethacin is variable, depending on the postnatal and gestational ages of the infant. In this context, we analyzed our data on infants of less than 30 weeks' gestational age and less than 1200 gm at birth with and without SPDA, and the subsequent morbidity and outcome with regard to management.

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Accepted for publication 8 April 1990.

Methods

Thirty-nine infants with a birth weight less than 1200 gm and less than 30 weeks' gestation who were admitted to the neonatal intensive care unit of Milwaukee County Medical Center from January 1, 1987, to June 1, 1988, were included in the study. Charts were reviewed for the presence or absence of SPDA and for the following variables: oxygen days, ventilation days, hospital days, and incidence of BPD, IVH, and necrotizing enterocolitis. SPDA developed in 21 infants and the remaining 18 did not suffer SPDA. The SPDA group was further classified into four groups, depending on the management adopted. Group 1 had fluid restriction and diuretics only. Group 2 was treated with only indomethacin. Group 3 underwent surgical ligation after failure of indomethacin. Group 4 was treated by ligation primarily, without resorting to medical management. The decision to manage infants differently depended on the individual preference of the consultant. This gave us an opportunity to compare these groups.

SPDA was diagnosed if there was a systolic murmur with bounding pulses and hyperactive precordium. Echocardiogram was used to assess the possible existence of other congenital cardiac defects and to confirm the diagnosis of patent ductus arteriosus, if the LA:AO ratio in the M-mode echocardiogram was greater than 1.2. In a few selected cases, pulsed Doppler was also used to confirm the diagnosis. The ductus was considered closed if the diastolic pulsewave was not negative (retrograde), the LA:AO ratio was less than 1.1, and other clinical signs such as the murmur and hyperactive precordium disappeared. The group treated with fluid restriction (Group 1) received 90 to 100 ml/kg of body weight per day of fluids, along with 1 mg/kg of Lasix daily. The indomethacin group (Group 2) received 0.1 mg/kg IV every 12 hours for three doses, along with fluid restriction to 100 to 110 ml/kg/day during that period. Contraindications to indomethacin use were thrombocytopenia (platelet count < 60,000); a blood urea nitrogen, > 10.7 mmol/L; creatinine, > 123 μmol/L; and hyperbilirubinemia defined as a serum bilirubin level > 101.69 μmol/L. BPD was defined as oxygen dependency for up to 28 days of age. There were no cases of necrotizing enterocolitis.

Results

Comparison of the data between the SPDA and control groups revealed that the morbidity was higher in the SPDA patients. They had more ventilation days, oxygen days, and hospital days, and a higher incidence of BPD. A higher incidence of respiratory distress syndrome (RDS) was also seen in the SPDA group. There were no differences in the birth weights between the two groups, suggesting that RDS contributed to the higher morbidity in the SPDA group. There was no difference in the incidence of IVH between the two groups. SPDA did not develop in 46.2% (18/39) of the total number of infants (Table 1).

Analysis of the different variables among the four groups was carried out by analysis of variance, and intergroup comparisons were done by two-tailed *t* tests. These data indicate that Group 3 infants were of lower birth weight. Group 1 infants had the highest birth weights and the least morbidity. The incidence of IVH did not differ among groups. The incidence of BPD did not differ among the indomethacin (Group 2), indomethacin and ligation (Group 3), and ligation only groups (Group 4), but was absent in the fluid restricted (Group 1) group (Table 2).

To evaluate the effect of surgery, the groups were recombined into surgical (Groups 3 and 4) and nonsurgical (Groups 1 and 2) groups. The surgical group had a lower birth weight and displayed significantly increased morbidity. The day of closure was earlier for the surgical group than for the nonsurgical group. However, when the day of closure was used to correlate oxygen with ventilation days, no significant correlation was detected among the SPDA infants overall. All infants in the surgical group had severe RDS and BPD. Further analysis of the nonsurgically managed SPDA groups and the control (no patent ductus arteriosus) group was carried out and no difference was detected in the morbidity or in any other variables. Thus, surgery in combination with low birth weight and the presence of RDS may have contributed to the increased morbidity in our group. Multiple-regression correlation analysis was used to compare birth weight, oxygen days, and ventilation days with the day of closure of the ductus. No significant correlation was found between the day of ductus closure and the oxygen

TABLE 1. *Data for SPDA and control groups and the nonsurgical and surgical management groups of SPDS.*

Variables	SPDA (N = 21)	Control (N = 18)	Nonsurgical (N = 10)	Surgical (N = 11)
BW (gm)	841 ± 210	893 ± 150*	1017 ± 134†	682 ± 122
Oxygen days	52.8 ± 35‡	17.6 ± 22	28.6 ± 26†	72.5 ± 29
Ventilation days	34 ± 27‡	6.1 ± 8.9	11.8 ± 13†	52.4 ± 21
Hospital days	88 ± 28‡	68 ± 9.3	73.5 ± 20†	102 ± 27.5
BPD	16†	6	5	11
RDS	16‡	5	5	11
IVH	4‡	8	1	3

N.B. Numbers expressed are the means ± SD, except for the incidences of BPD, RDS, and IVH.
‡$P < 0.05$ between SPDA and control groups; *$P < 0.05$ between control group and nonsurgical management groups; †$P < 0.05$ between nonsurgical and surgical groups.
SPDA = symptomatic patent ductus arteriosus; BW = birth weight; BPD = bronchopulmonary dysplasia; RDS = respiratory distress syndrome; IVH = intraventricular hemorrhage.

TABLE 2. *Outcome of management of symptomatic patent ductus arteriosus in 21 infants.*

Variables	Fluid restriction (N = 3)	Indomethacin (N = 7)	Indomethacin and ligation (N = 6)	Ligation (N = 5)
BW (gm)	1098 ± 47	982 ± 152†	660 ± 87	710 ± 141
Oxygen days	3.3 ± 3.5*	42 ± 21.9	72 ± 35	73 ± 24.9
Ventilation days	1.6 ± 0.5	17 ± 13	8.5 ± 16.9	56.4 ± 26
Hospital days	50.6 ± 12*	79.6 ± 8.7†	104.3 ± 26.2	101 ± 32
BPD	0	5	6	5
RDS	0	5	6	5
IVH	0	1	2	1

N.B. Numbers expressed are the means ± SD except for the incidences of BPD, RDS, and IVH.
*$P < 0.05$ between the fluid restriction only and indomethacin only group; †$P < 0.05$ between indomethacin plus ligation and ligation only groups.
BW = birth weight; BPD = bronchopulmonary dysplasia; RDS = respiratory distress syndrome; IVH = intraventricular hemorrhage.

or ventilation days (oxygen days, $r = 0.02$, $P = 0.7$; ventilator days, $r = 0.04$, $P = 0.69$). Thus, whether accomplished medically or surgically, the time of closure of the ductus arteriosus had no bearing on subsequent morbidity.

Discussion

SPDA is known to contribute to the respiratory morbidity of preterm infants. It has also been implicated as one of the causes of necrotizing enterocolitis, IVH, and BPD [1–4]. Moreover, closure of ductus arteriosus is associated with significant improvement in the lung mechanics [7]. It is thus natural to speculate that the prophylactic closure of the ductus arteriosus should be helpful in the management of very-low-birth-weight infants. However, Merritt et al [8] in a study which used indomethacin in the treatment of SPDA was not able to demonstrate any difference between control groups and early patent ductus arteriosus intervention groups in terms of the total number of hours on ventilation or on oxygen. No statistically significant difference was noted in the mortality either. Mahony et al [9] reported on the effect of prophylactic indomethacin in very-low-birth-weight infants with subclinical patent ductus arteriosus without large left-to-right shunts. In their group of infants of less than 1000 gm, a significant difference was noted in the group who received prophylactic indomethacin with regard to decreased duration of oxygen exposure and fewer days required to regain birth weight. However, no difference was noted in the group with a birth weight greater than 1000 gm. In another study [10], indomethacin or placebo was used at a mean age of 15 hours in infants weighing between 700 and 1300 gm. There was no difference in the morbidity between the groups, and this was attributed to the low incidence of large shunts (21%) in the control groups. Prophylaxis has an unclear role in the management of ductus arteriosus with regard to reducing morbidity in very-low-birth-weight infants. In our infants we did not use indomethacin prophylactically but prescribed it only after SPDA developed. Our results indicate that the surgically managed group who received indomethacin had the highest morbidity. The question arises whether it is surgery or other factors such as delayed closure of ductus that give rise to this phenomenon. Preterm infants are more susceptible to complications following surgery (e.g., hypothermia, apnea, anesthetic risks) [11], and this is borne out in our infants who had severe RDS and were generally of lower birth weight. All these factors may be responsible for the increased morbidity in this group. The day of closure of the ductus arteriosus was not shown to be an important factor in the number of oxygen or ventilation days.

The medically managed SPDA infants did not exhibit increased morbidity compared with controls. Successful closure of the ductus arteriosus occurred in seven of 13 (53.8%) infants who had received indomethacin. Those infants with SPDA who did not respond to indomethacin are the ones who had increased morbidity, and we can only speculate that they would not have responded to indomethacin used prophylactically. Only 11 of the 39 (28.2%) infants underwent surgery, and we do not believe that the prophylactic use of indomethacin would have been helpful in reducing morbidity. Recently, Cassady et al [12] reported the results of early prophylactic ligation of the ductus arteriosus on the first day of life in very-low-birth-weight infants. They observed no difference in the pulmonary morbidity in these infants compared with control infants. Others have urged caution in the prophylactic management of ductus arteriosus in low-birth-weight infants [13].

The response to indomethacin is reported to be influenced by gestational age, birth weight, postnatal age, and postconceptional age, as well as adequate plasma levels of the drug [14–18]. Indomethacin, in the treatment of patent ductus arteriosus, has been well studied and no major complications have been reported [19,20].

In our experience, infants with a birth weight less than 700 gm (24–25 weeks) are the ones who require surgery if SPDA develops. Severe RDS often develops in these infants, and there is a strong association between lung immaturity and the development of SPDA. The combination of RDS and surgical intervention may be responsible for the high morbidity in this group, despite successful ductus ligation.

Our results indicate that, when SPDA develops in infants, fluid restriction and indomethacin should be tried before surgical intervention is attempted, as suggested by Gersony [21]. This is especially true for infants with birth weights greater than 800 gm. Whether the early ligation of ductus arteriosus in infants under 800 gm would decrease the long-term morbidity needs to be studied.

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ORAL HEALTH CARE OF SAUDI LEUKEMIC PATIENTS

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تتزايد الحاجة في المملكة العربية السعودية لتحسين العناية بصحة الفم، مع اختلاف هذه الحاجة من فئة إلى أخرى. فحاجة المصابين بابيضاض الدم إلى العناية بأسنانهم تفوق حاجة الأصحاء إلى ذلك، نظراً لما يرافق مرضهم من مضاعفات خطيرة في الفم ومن عجز جسدي يحول دون المحافظة على نقاء أسنانهم من اللويحات. ونظراً لنقص القوى العاملة في مجال العناية بالأسنان فمن المحتمل أن يتلقى مرضى ابيضاض الدم في المملكة العربية السعودية قسطاً ضئيلاً من العناية السنية المتخصصة لا يفي بالغرض. وقد أظهرت دراسة مبدئية على ٣٠ حالة ابيضاض دموي من أربعة مستشفيات كبيرة في الرياض مَنَاسب عالية من اللويحات والحصيات السنية ونزف اللثة. بلغ مَنْسَب اللويحة لدى ٥٤٪ من المرضى أكثر من ٨٠٪ أثناء الإقامة في المستشفى، في حين بلغ لدى ٣١٪ من المرضى أكثر من ٨٠٪. كان جميع مرضى ابيضاض الدم الذين تم فحصهم يعانون من تقرحات في الفم أو خمج فطري أو تضخم اللثة أو نزفها، مما استدعى مزيداً من العناية الطبية. تشير هذه الدراسة إلى أن المرضى السعوديين المصابين بابيضاض الدم بحاجة ماسة إلى عناية أفضل بصحة الفم. وتشتد الحاجة إلى المزيد من مراكز الأسنان التخصصية المزودة بالأكفياء من أخصائيي صحة الأسنان لتقديم العناية بصحة الفم لهؤلاء المرضى.

There is a growing demand in Saudi Arabia for better oral health care; however, the need varies from one group to another. Patients with leukemia require more dental care than do healthy subjects because of associated serious oral complications and physical disabilities in maintaining plaque-free teeth. Because of a dental manpower shortage, leukemic patients in Saudi Arabia are likely to be receiving less specialist dental care than they require. A pilot study of 30 leukemic patients from four major hospitals in Riyadh showed high indices of plaque, calculus, and gingival bleeding. While hospitalized, 54% of the patients had a plaque index of greater than 80%, whereas 31% of the patients had a bleeding index of greater than 80%. All leukemic patients examined had either oral ulcerations, fungal infection, gingival enlargement, or gingival bleeding that necessitated further medical attention. This study indicates that Saudi leukemic patients desperately require better oral health care. Additional specialist dental centers staffed by appropriately trained dental personnel are urgently needed to provide oral health care for these patients.

Leukemia is characterized by neoplastic proliferation of one of the blood-forming cells [1]. It is classified as lymphocytic, myelocytic, or monocytic according to the cell type, and is acute or chronic depending on the nature of onset. If untreated, all forms of leukemia are fatal. Death usually results from bone marrow replacement of the normal hematopoietic tissue with leukemic cells [2]. Treatment includes chemotherapy, radiotherapy, blood transfusion, and bone marrow transplantation with an overall emphasis on infection control [3].

Because of the higher survival rate and the related side effects of chemotherapy, leukemic patients now require more oral health care [4]. Terminally ill patients have a high prevalence of oral symptoms and a high incidence of candidiasis

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Accepted for publication 12 May 1990.

[5]. Consequently, leukemic patients are included in the category of patients with special dental needs.

Clinically, some oral features of leukemia are related to the disease process. Hemorrhage and anemia result from thrombocytopenia and erythrocytopenia, respectively [6]. Widespread infection is due to the replacement of the normal hematopoietic tissues by immature leukocytes. A general mucosal pallor, gingival hypertrophy, ulceration, infection, pain, and extensive petechial bleeding are other frequent oral findings [7].

Other oral features of leukemia are attributable to the widespread use of chemotherapy. Chemotherapeutic agents are not tumor specific; they destroy leukemic cells as well as normal cells, thus further weakening the body's defenses. Patients become more susceptible to infection, hemorrhage, anemia, nausea, vomiting, and xerostomia. Chemotherapy has been reported to cause infection, mucositis, and hemorrhage in 68% of leukemic patients [6].

Oral ulcerations in myelosuppressed leukemic patients may lead to serious systemic complications because they offer an easy portal of entry for microorganisms [8]. Candidal infection is another serious consequence of the extensive antibiotic and steroid therapy that are usually prescribed for these patients. A high standard of oral health care is a minimum requirement for the general well-being of these patients.

The aim of the present preliminary study was to determine the dental treatment needs of Saudi leukemic patients and to assess how well these are being met in local hospitals.

Material and Methods

Forty-nine Saudi patients with acute leukemia, who were admitted during a three-month period to four major hospitals in Riyadh, made up the study population. Nineteen patients were later excluded because they were discharged, died, or declined to participate further. Fourteen female and 16 male patients (aged 17 to 68 years) completed the study. Thirty healthy control subjects were randomly selected from the periodontal department at the College of Dentistry, Riyadh. They were first-time attenders (aged 19 to 52 years) and consisted of 14 female and 16 male subjects.

All patients underwent a visual oral examination during which the status of the cheek mucosa, lip, tongue, floor of the mouth, palate, and the anterior pillar of the fauces was recorded. Six pocket depth readings (from the gingival margin to the base of pocket) were taken for each of the six teeth used for the Oral Hygiene Index [9]. These were the upper right first molar, upper right central incisior, upper left first molar, lower left first molar, lower left central incisior, and lower right first molar. Plaque [10] and bleeding on probing indices [11] were recorded for every tooth in the mouth as the mean of its four surfaces. The presence or absence of plaque or bleeding at every tooth surface was scored as 1 or 0, respectively. The four scores from all the teeth were summed, divided by the number of surfaces examined, and multiplied by 100 to yield the index percentage for each subject. For statistical analysis and for comparing our findings with other published data, the percentage figures were converted to a numerical scale between 0 and 5, as follows: a unit score was allocated for every 20 percentage points, the maximum value of 100% being allocated for a score of 5. The status of the calculus was assessed by the component of OHI-S index using a score range of 0 to 3 for all the teeth [9].

Results

Of 30 leukemic patients who completed the study, 54% had a plaque index greater than 80%, whereas 31% had a bleeding index greater than 80% (Figure 1). The numerical mean for the plaque index was 4.30, whereas the mean for the bleeding index was 3.21. This compares with a mean plaque score of 1.9 and a mean bleeding score of 1.0 in the control group. The calculus and pocket depth means in the leukemic patients were 1.25 and 3.2 mm, respectively (Table 1). In the control group, the mean pocket depth was 2.9 mm, but calculus scores were not recorded.

To assess the inflammatory response in leukemic patients in relation to plaque data, the three indices and pocket depth measurements were further analyzed statistically by the Spearman Rank correlation coefficient. The mean pocket depth was significantly correlated with the calculus index ($r = 0.53$) (Table 2). The plaque index was also significantly correlated with both the

TABLE 1. *Medians, means, standard deviations, and ranges of the four recorded clinical parameters.*

Index	Median	Mean	SD	Range
Calculus index	1	1.25	0.92	0–3
Bleeding index	3	3.21	1.52	1–5
Plaque index	5	4.30	1.06	1–5
Mean pocket depth	3.3	3.2	0.67	1.5–4.2

TABLE 2. *Statistical analysis of the four recorded clinical parameters by the Spearman rank correlation coefficient.*

Index		Calculus index	Bleeding index	Plaque index	Mean pocket depth
Calculus index	*r*	1	0.35	0.31	0.53
	p	–	NS	NS	<0.01
Bleeding index	*r*	0.35	1	0.84	0.12
	p	NS	–	<0.001	NS
Plaque index	*r*	0.31	0.84	1	0.66
	p	NS	<0.001	–	<0.01
Mean pocket depth	*r*	0.53	0.12	0.66	1
	p	<0.01	NS	<0.01	–

bleeding ($r = 0.84$) and the mean pocket depth ($r = 0.66$) (Table 2). The bleeding index scores, however, did not correspond directly with the plaque index scores, which is possibly attributable to the immunosuppression seen in leukemic patients. Many patients with high plaque scores had lower bleeding scores (Figure 1). No correlation between plaque and bleeding scores was evident until a plaque score of 4 was reached (Figure 2).

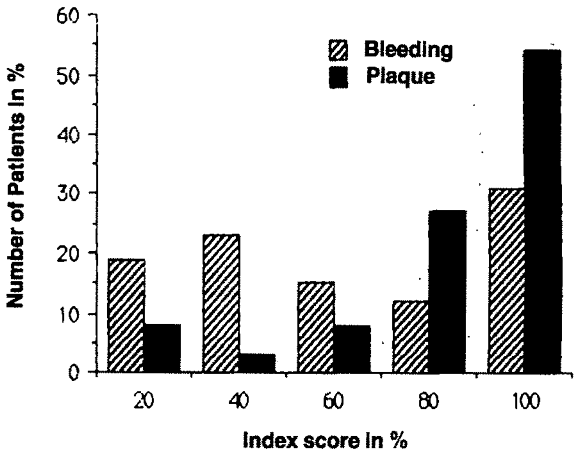

FIGURE 1. Comparison of the percentage of patients and the scores for plaque and bleeding indices.

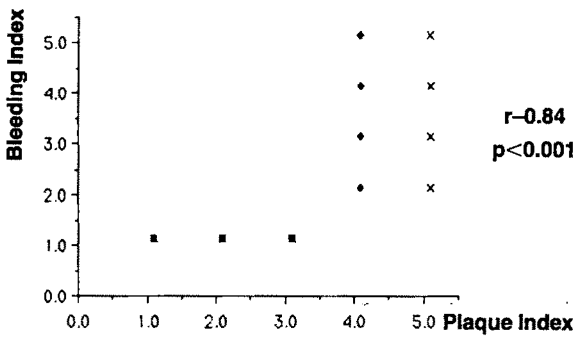

FIGURE 2. Correlation of the plaque index with the bleeding index.

Clinical examination revealed that most patients had general mucosal pallor and bulbous erythematous interdental papillae. Throat and mouth ulcerations were noted in 10 patients (33%). Active caries was found in 18 patients (60%). Two patients had more than one episode of toothache during their hospitalizations. Candidiasis was diagnosed clinically in 22 patients (73%). The lesions appeared as white patches and were mostly located on the surface of the tongue, palate, and cheek. Xerostomia and fissured tongue were other frequent symptoms. Pale yellow gingiva was noted in three patients and was related to preexisting liver damage. Generalized gingival enlargement was noted in only seven patients (23%), but localized papillary enlargement was common. In one hospital, eight patients were given Cepacol mouth wash containing 0.005% cetylpyridinium and 14.7% ethyl alcohol, but this did not lead to improved oral hygiene.

Discussion

Patients with leukemia must be monitored rigorously during chemotherapy. Strict infection control is as important as providing the necessary platelets and blood cells. Preventive measures should include local antibiotic therapy and intensive patient education in the maintenance of oral hygiene [3].

The primary goal of dental care in these patients should be aimed at: (1) identifying and treating oral problems before chemotherapy; (2) preventing complications during chemotherapy; and (3) providing comprehensive dental care following chemotherapy. Effective dental care for the leukemic patient should begin early and prior to the start of any therapy in general and chemotherapy in particular. The patient's oral health status should be assessed, full caries and periodontal charting recorded, and full mouth radiographs taken. Treatment should include thorough oral prophylaxis and repeated instructions in proper oral hygiene. Teeth with a poor prognosis should be extracted, carious teeth restored, unsatisfactory restorations replaced, and ill-fitting appliances renewed. Impacted teeth in communication with the mouth should be removed if practical. Any orthodontic bands and wires should also be removed to avoid further irritation and bleeding. Patients in remission should receive regular dental care to prevent acute dental episodes during any future myelodepression [3,12].

An oral care protocol for leukemic patients with chemotherapy-induced complications was devised by Debiase and Komives in 1983 [8]. They recommended that patients with mild mucositis should brush their teeth with a soft nylon brush and rinse with one part hydrogen peroxide in four parts saline twice daily. A dentifrice is not recommended because it may cause pain and irritation. Patients receiving chemotherapy should avoid flossing unless they are extremely adept in the technique. If mucositis is severe, the oral cavity should be gently cleaned with gauze dipped in a solution of 5 ml of sodium bicarbonate and 500 ml of saline twice a day. Patients with mucositis should also avoid commercial mouth rinses because of their high alcohol and phenol content [8].

The Saudi leukemic patients in our study were found to have high plaque, calculus, and bleeding on probing scores compared with healthy control subjects. Leukemic patients are medically compromised and should follow a higher standard of oral hygiene than healthy individuals. Conversely, Aldred et al [13], who used the Oral Hygiene Plaque/Debris index, reported a mean plaque score of 1.97 among terminally ill British patients (corresponding to 2.95 in our 0 to 5 scale), which is much lower than our score of 4.30 in Saudi patients. Similarly, candidiasis was diagnosed in 73% of the Saudi leukemic patients, compared with 56% in the terminally ill British patients [5]. The high scores for plaque, bleeding, and *Candida* infection among the Saudi leukemic patients indicate a lack of sufficient dental health care. *Candida albicans* has been reported to be present commensally in the oral flora of between 29 and 50% of healthy adults, but was increased in immunocompromised patients [14]. On the other hand, Williams et al [15] felt that *candidal* infection resulted from poor oral hygiene and emphasized that mouth care should commence long before any antifungal therapy. Improving the standard of oral hygiene appears to be an essential preventive measure against candidal infection, especially when antifungal treatment is not effective in such patients [16]. In our study, active caries were found in most patients (60%) with little or no attention paid to oral hygiene. Education, motivation, and oral hygiene instructions had not been provided because neither the physician nor the nursing staff were aware or trained for this type of care. Interestingly, the most acute oral infections following chemotherapy are associated with preexisting periodontal disease [16]. Acute periodontal abscess is known to cause high fevers but relatively little suppuration and pain [12]. Lack of pain among these patients does not indicate healthy dentition; thus, thorough periodontal and dental assessment before, during, and after chemotherapy is a must. Cepacol mouthwash contains 14.7% alcohol and this further traumatizes an already damaged mucosa. Chlorhexidine-containing mouth rinse was not available to any of these leukemic patients. Chlorhexidine mouth rinses contain no alcohol and, when used twice a day, have proved to be a reliable antiplaque agent [17]. It is therefore recommended in the management of leukemic patients.

It is clear from our findings that Saudi leukemic patients are in desperate need of specialized dental health care. An ample number of special dental centers must be provided for treating medically compromised patients. These centers should be available not just in hospitals but also at the community level, and should be sufficiently equipped with appropriately trained staff. It is not only important to remove plaque, treat oral infection, and relieve the pain of ulceration but also the dental specialist must know how to liaise between oncologists, physicians, and radiotherapists in determining the safe approach and timing of dental treatment. The involvement of appropriately trained nursing staff in the regular dental care of medically compromised patients is an issue which is least discussed but ironically most important.

Acknowledgments

We thank our colleagues at the various hospitals of Riyadh who offered access to their patients and the staff of the Department of Photography, College of Dentistry, Riyadh, for preparing the illustrations.

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EARLY MOBILIZATION FOLLOWING ANTERIOR FIXATION WITH BONE GRAFT AND METAL PLATE IN TRAUMATIC CERVICAL FRACTURE DISLOCATIONS

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تمت معالجة ثماني عشرة حالة كسر خلعي رضحي جراحيا باستخدام طريقة تشمل مباشرة العملية من ناحية العنق الأمامية ثم استئصال القرص، وزرع طعم عظمي والتثبيت بصفيحة معدنية. تم تحريك المرضى في وقت مبكّر لتفادي حدوث المضاعفات المعتادة كقروح الفراش، والخثار الوريدي العميق، والانصمام الرئوي، والخمج الصدري، والتقفع. وبعد عامين من المتابعة، لم يعان أي مريض من الخمج المُوضعي، أو ارتخاء براغي التثبيت، أو التدهور العصبي، أو عسر البلع، أو استمرار خزل العصب الحنجري. من فوائد هذه الطريقة، التي سبق تأييدها في بعض المقالات، خفض نسبة المراضة وزمن الاستشفاء فضلاً عن تخفيف الطلب على خدمات الهيئة العاملة كما هي الحال في مرضى الشلل الرباعي.

Eighteen cases of traumatic fracture dislocation were managed surgically using a technique which involved an anterior cervical approach followed by discectomy, bone graft, and insertion of a metal plate. The patients were mobilized early to prevent the usual complications of bedsores, deep vein thrombosis, pulmonary embolism, chest infection, and contractures. After more than two years of follow-up, no patient has had problems with local infection, screw loosening, neurological deterioration, dysphagia, or persistence of laryngeal nerve paresis. The benefits of this technique, already endorsed by some authors, include reduced morbidity and hospitalization as well as decreased demand on the staff, particularly as required by quadriplegic patients.

Cervical injury commonly occurs in the young, and is associated with a high incidence of quadriplegia. Treatment is aimed at preventing further neurological loss as well as other posttraumatic complications such as bedsores, deep vein thrombosis, pulmonary embolism, chest infection, and prolonged hospitalization, in addition to promoting early rehabilitation. The main hurdle is the instability of the spine. Traditional fixative methods such as bone graft followed by continuous skeletal traction require sophisticated beds like the Stryker frame and skilled nursing care to prevent such complications. To overcome these shortcomings we have adopted the technique of anterior discectomy and osteosynthesis with bone graft and screw metal plate fixation to achieve early and easy mobilization of patients with and without neurological deficit. The scientific basis and advantages of this procedure are discussed. The cases reported support our recommendations.

Material and Methods

Eighteen cases of traumatic unstable cervical fracture-dislocations have been encountered at King Fahad Hospital, Medina Munawara, since 1987 and comprise our study group. Cases of C1 and C2 injuries were excluded because the technique of fixation we used cannot be performed for such fractures. The technique of bone graft and metal plate osteosynthesis was used in all 18 patients (Table 1). There were 15 males and 3 females and this male preponderance probably reflects the driving law in Saudi Arabia where

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Accepted for publication 3 June 1990.

TABLE 1. *18 Cases of anterior cervical fixation.*

				Upon admission			Postoperative		
Case No.	Age (yr) sex	Origin	Level	Neurological condition	Respiratory support	Cardiovascular abnormality	First day of mobilization	Neurological improvement	Mortality
1	40,M	RTA	C6/7	Quadriplegia below lesion	–	Bradycardia	17	No	Dead
2	60,M	RTA	C3/4	Elbow and hand weakness	–	–	10	Improved	–
3	30,M	Fall of heavy object	C4/5	Total quadriplegia	Ventilated	Bradycardia	–	No	Dead
4	60,M	RTA	C5/6	–	–	–	1	–	–
5	50,M	RTA	C6/7	–	–	–	1	–	–
6	28,M	RTA	C4/5 C6/7	Total quadriplegia	–	–	13	–	–
7	30,M	RTA	C4/5	Total quadriplegia	Tracheostomy, ventilated	Bradycardia	41	No	–
8	40,M	RTA	C6/7	–	–	–	10	–	–
9	55,M	RTA	C4/5	–	–	–	10	–	–
10	70,M	RTA	C5/6, C6/7	Brown-Sequard syndrome	–	–	17	Improved, able to walk	–
11	19,M	RTA	C4/5	–	–	–	1	–	–
12	19,M	Fall from camel	C6/7	–	–	–	1	–	–
13	40,F	RTA	C5/6	Upper limb weakness	–	–	4	Partially improved	–
14	40,F	Fall	C4/5	Upper limb weakness	–	–	2	Improved	–
15	55,M	RTA	C5/6	Quadriplegia below lesion	–	Bradycardia	–	No	Dead
16	35,M	Fall	C7/1	Quadriplegia below lesion	–	Bradycardia	16	No	–
17	30,M	RTA	C4/5	Total quadriplegia	Ventilated for 38 days	Bradycardia	54	No	–
18	35,M	RTA	C5/6	Quadriplegia below lesion	Ventilated	Bradycardia	Still ventilated	No	–

RTA = road traffic accident.

women are not allowed to drive. The most common age group affected was between 19 and 40 years (66%), and the most frequent vertebral level was C4/5 (39%). The main presenting complaints were pain in the neck, inability to move the limbs, loss of sensory feeling, and brachialgia. Eight patients had complete quadriplegia with sensory deficit below the lesion, and five had partial neurological deficit, more often involving only the upper limbs. Respiratory support was required in four, and cardiovascular instability was noted in seven. Associated injuries of the head, chest, abdomen, and limbs were seen in eight. Nine had urinary retention. Plain x-ray studies supplemented with computed tomographic (CT) scans were carried out to detect the level and extent of dislocation, and any hematoma formation and bone fragments inside the vertebral canal.

Surgery was performed as soon as possible, irrespective of the degree of motor or sensory deficit. Twelve had fixation within 1 week, three within 2 weeks, and three within 3 weeks of admission. The longest stay in bed before mobilization with a cervical collar was 17 days, even for patients with complete quadriplegia, not requiring ventilation.

Treatment

On admission all patients were placed in Gardner-Wells skull traction to reduce the dislocation. If subsequent x-ray studies revealed persistent dislocation, despite traction with increased weights and extensor neck posturing, manipulative reduction was attempted either in the radiology department with the patient sedated or in the operating theater with the patient under general anesthesia and muscle relaxants given before surgery. We achieved reduction in all patients using the closed method.

After positioning of the patients, before skin incision, x-ray studies were repeated to confirm the reduction. Through the standard Cloward [1] approach, the affected level was exposed and verified by placing a lumbar puncture needle within the disc space with the help of the image intensifier. Total discectomy with scraping of hyaline cartilage under microscope control and using the drill was carried out. A careful search was made for extruded disc fragments, as found in two of our cases. Posterior common cervical ligament was left in situ unless torn. The bone graft was taken from the iliac crest, fashioned to the correct size and shape of the empty disc space, and gently hammered in place. Skeletal traction was released. A metacarpal plate and screws of appropriate sizes were selected (Figure 1). The appropriate length of the screws was determined using a simple vertical metallic stick introduced into the disc space which indicated the anteroposterior diameter of the vertebral body. Using an air-powered or hand drill, holes were made into the vertebral bodies above and below the bone graft space, corresponding to the placement of the holes in the metal plate. Osteosynthesis was performed by screwing the plate firmly in place. An x-ray study was done to confirm satisfactory reduction and osteosynthesis (Figure 2). The wound was closed in layers with a Redivac drain and cervical collar applied. All patients received prophylactic antibiotics. Patients were nursed in bed, usually for one week, and slowly mobilized with the collar on once x-ray study confirmed stability of the lesion. Fixation of two levels was done in two of our patients (Figure 3).

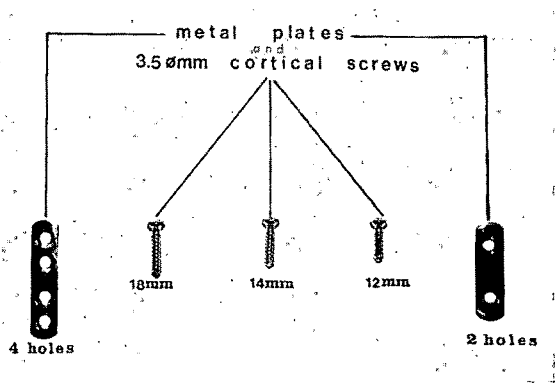

FIGURE 1. Metal plates and screws of different sizes.

Results

There was no incidence of infection in either the wound or disc space, screw loosening, or cerebrospinal fluid leak, though patients did suffer hoarseness which abated gradually. None had neurological deterioration. Three of seven patients presenting with cardiac problems died, but only one required ventilation at the time of admission. Patients with bradycardia most probably had initial lesions of the autonomic nervous system. The three reported deaths are attributed to irreversible damage of the sympathectomy effect often encountered with high-grade cervical spinal cord lesion. One of our patients with total quadriplegia and respiratory failure required tracheostomy on admission, as cardiac arrest developed when nasotracheal intubation was attempted and was due to vagal stimulation unopposed by sympathetic loss. He underwent fixation without postoperative infection, despite the tracheostomy, and on the 80th day was transferred, while maintained on a ventilator, to a peripheral hospital. One of the nine patients with urinary retention regained full bladder control following surgery. Some degree of improvement was noted in the four who presented with only upper limb weakness. Six who had no deficit and three with

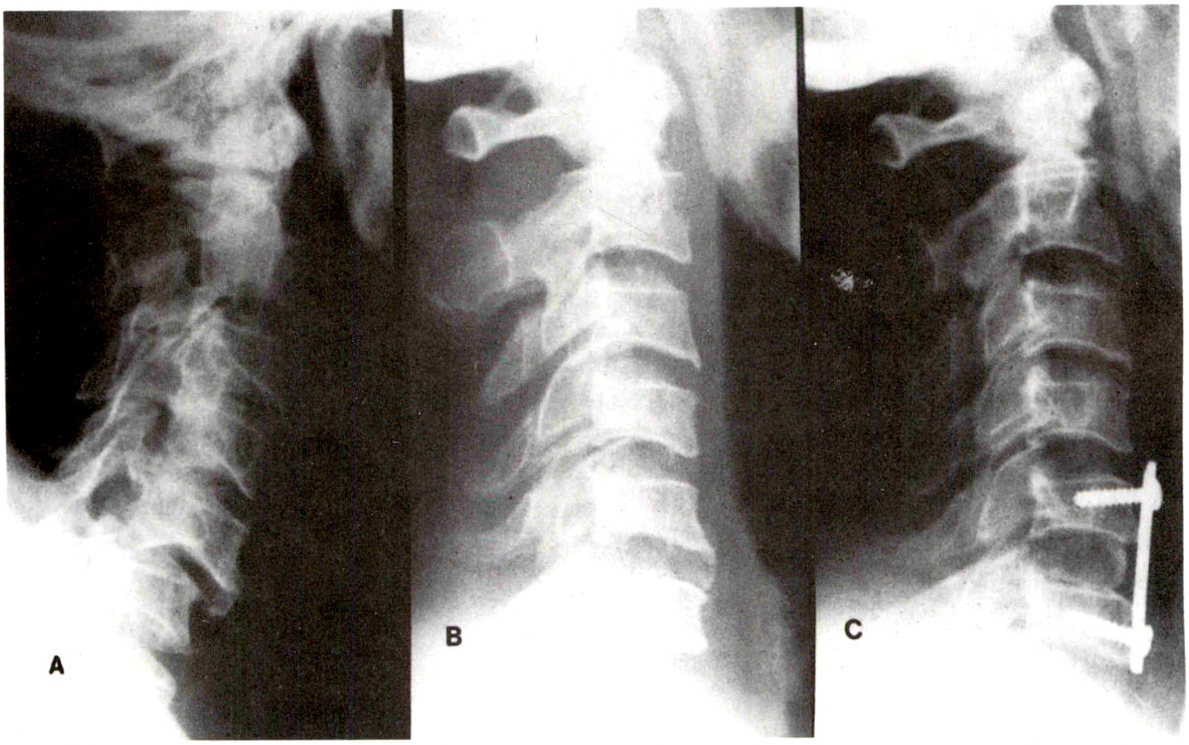

FIGURE 2. (A) C5/6 fracture-dislocation. (B) Repeat x-ray study after skeletal traction. (C) Postoperative x-ray study showing fixation with bone graft and metal plate.

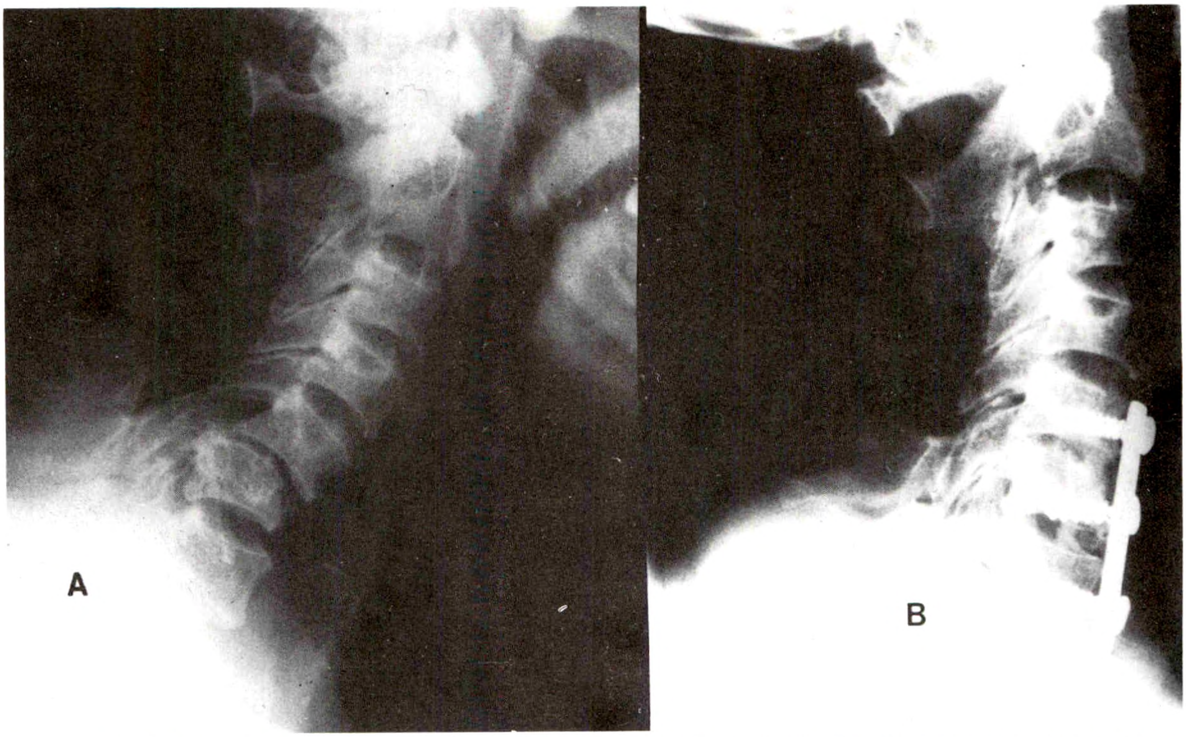

FIGURE 3. (A) C5/6, C6/7 fracture dislocation. (B) Postoperative x-ray study showing fixation with bone graft and metal plate at two levels.

mild weakness were discharged within 3 weeks. Four with severe neurological deficits were mobilized in wheelchairs and later transferred to rehabilitation centers or peripheral hospitals.

Discussion

Early mobilization following severe cervical injury definitely reduces morbidity and mortality. It also allows for early rehabilitation and return to normal activities, ensuring a decent quality of life in particular for young quadriplegics. To achieve this goal, stable fixation is essential. Such a procedure should be free of the risk of further neurological deterioration, and at the same time treat associated causes of the neurological deficit such as protruded disc, hematoma, and bone fragments inside the vertebral foramen.

There are several methods of cervical fixation using anterior, posterior, or combined approaches. An increasing number of surgeons are favoring the anterior approach because it also provides for removal of a traumatized or protruding disc. It also facilitates a relatively strong and stable fixation with good alignment, avoiding the several disadvantages associated with the posterior approach, for example: (1) weakening of the strong posterior group of muscles; (2) inability to remove protruded discs; (3) the shearing effect created by dislocation weakens the anterior supports and may necessitate a further anterior approach [2]; (4) technical pro-blems such as screwing pedicles, wiring lamina in the presence of fractures, and breakage of wires; and (5) the necessity of prolonged external immobilization.

The anterior approach with discectomy and bone graft without plating also requires external immobilization or sophisticated braces. Wearing a simple, comfortable cervical collar following osteosynthesis, as used in our patients, proved the obvious advantage of our method, because it allowed patients to be mobilized safely and quickly. We insisted on all our patients wearing collars for three months, minimum.

We have used this technique in 18 patients of different sex and age groups, with injuries at different levels, extending from C3 to T1 and with varying neurological deficits, including inpatients on ventilators with tracheostomy. Our study suggests early surgery in patients with cardiovascular problems should be approached with caution, as three of five of such patients died compared with none of the two who underwent a delayed procedure.

Finally, anterior cervical fixation with a bone graft and metal plate can be used even in cases of dislocation involving articulocapsular lesions damaging the three components of the articulation [2] and also in cases of dislocation involving more than one level either adjacent or distant, as in two of our cases (Nos. 6 and 10). Following adequate fixation, mobilization is done as soon as possible to prevent the complications associated with total quadriplegia. We have not encountered either infection or screw loosening, which are the two main objections raised by some authors against this procedure [2].

This procedure is simple, requiring little sophisticated equipment. Our experience parallels that of Lesoin et al [2,3] who describe the procedure for fracture–dislocations as safe and effective for early mobilization without significant complications. We are convinced that this procedure leads to reduced morbidity associated with prolonged immobilization, as well as shortening the patient's hospital stay and lessening strain on the nursing and rehabilitation staff.

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THE RADIOGRAPHIC FEATURES OF PULMONARY TUBERCULOSIS OBSERVED FOR THE WESTERN REGION OF SAUDI ARABIA

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درسنا الصور الشعاعية لسبعمائة وأربعة عشر (٧١٤) مريضاً (٤٨٦ ذكراً، ٢٢٨ أنثى) يعانون من درن رئوي مثبَت. تراوحت أعمار أغلبهم بين ١٥ و٤٤ سنة، وشوهد المظهر الاعتيادي للدرن في الصور الشعاعية لدى غالبيتهم (٨٦,٨٪). كان جميعهم يعانون من مرض واسع النطاق في الرئتين، وكان الفص العلوي الأيمن أكثر المناطق إصابة. كانت العتامات المتنية والتكهف والانخماص شائعة. صودفت أنماط عديدة في الصور الشعاعية، وتباينت هذه الأنماط من صورة إلى أخرى، وحتى ضمن الصورة الواحدة إذ شوهد اجتماع نمطين أو أكثر. كما شوهدت مظاهر غير مألوفة لدى ١٣,٢٪ من المرضى شملت: عتامات منعزلة في الفص السفلي أو الأوسط أو اللسين، وصوراً طبيعية للصدر، وإصابات جنبية منعزلة، واعتلالاً معزولاً في الغدد اللمفاوية للمنصف أو للنقير، وآفات كتلية. يمكن تفادي تلف الرئتين الدائم إذا تم التعرف على مختلف السمات الشعاعية للدرن الرئوي في الحال وأعطي المريض معالجة مبكرة.

The radiographs of 714 patients (486 males, 228 females) with proved pulmonary tuberculosis (PTB) were studied. Most were between 15 and 44 years of age, and most (86.8%) exhibited the usual radiographic appearance of PTB. All had extensive bilateral lung disease, with the right upper lobe the most commonly involved. Parenchymal opacities, cavitation, and atelectasis were common. Many radiographic patterns were encountered, and these varied from one radiograph to the next and even within the same radiograph, with two or more patterns seen together. Unusual radiographic manifestations were found in 13.2% of the patients. These included isolated opacities in the lower lobe, middle lobe, or lingula; normal chest radiographs; isolated pleural effusions; isolated mediastinal or hilar lymphadenopathy, and mass-like lesions. Permanent lung damage could be avoided if the various radiographic features of pulmonary tuberculosis were promptly recognized, thus leading to early treatment.

Pulmonary tuberculosis (PTB) remains a major worldwide public health problem [1]. The failure to eliminate PTB, technically a curable and preventable disease, is due to many factors: the nature of the tubercle bacillus which allows it to remain dormant for extended periods, poor patient compliance with long-term treatment, the continued immigration of infected persons from other countries, and misdiagnosis by physicians [2].

The pattern of the disease may be modified by socioeconomic, genetic, dietary, and other poorly understood factors [3]. In addition, a changing pattern in the radiographic presentation of tuberculosis has been observed [4–6]. The radiographic appearance of PTB in Saudi Arabia has not been previously reported despite the high prevalence of the disease [7]. The purpose of our study was therefore to document the various radiographic features of PTB in the Western region of Saudi Arabia, and to see if they differ from those commonly described in the literature.

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Accepted for publication 16 May 1990.

Patients and Methods

Retrospective analysis of the initial chest radiographs was performed by one author (Dr. Al-Dabbagh) and the medical records were reviewed by all authors for the 714 patients with PTB. These patients had fulfilled the following criteria: (1) the presence of acid-fast bacilli (AFB) in smears or cultures of sputum or material obtained by bronchial washings or percutaneous or surgical open biopsy of pleural tissue, lymph nodes, or lung; (2) strong clinical and radiographic evidence of PTB, without bacteriological confirmation, but those cases which responded well to antituberculous treatment. The patients were divided into four groups according to age (Table 1).

All patients had at least one posteroanterior and one lateral radiograph. The following points were noted for each radiograph: (1) the distribution of the lung opacities; (2) the shape of the predominating pattern of opacities: homogeneous, inhomogeneous, acinar, ill-defined faint, nodular, or linear; (3) atelectasis; (4) cavitation, cavity wall thickness, and any fluid levels in the cavities; (5) pleural abnormalities, i.e., thickening, effusion, calcification, hydrothorax, or pneumothorax; (6) hilar or mediastinal lymph node enlargement and/or calcification; and (7) parenchymal calcification.

TABLE 1. *Age and sex distribtuion of 714 patients.*

Age group (yr)	Female	Male	Total
0–14	9	3	12 (1.7%)
15–29	118	186	304 (42.6%)
30–44	62	200	262 (36.7%)
45–80	39	97	136 (19%)
Total	228	486	714

There are many classifications of the radiographic features of PTB into usual and unusual characteristics using nonspecified methods [1,4–6,8,9], based primarily on authors' experience and other published classification schemes. Accordingly, we attempted to categorize the multiple associated lesions of PTB, such as upper lobe opacities with cavities, atelectasis, and calcifications, as usual manifestations. Unusual manifestations consisted of an isolated single lesion such as lower, middle, and lingular lobe opacities, effusion, or lymphadenopathies (Table 2). Since more than one pattern of opacity may occur in the same radiograph, the dominant pattern was recorded. All terms used in this manuscript are those described in the glossary of terms for thoracic radiology [10].

Results

The most common age group affected in our patient population was the 15 to 44-year-olds (Table 1). There were two 80-year-old patients, and the youngest patient was 19-months-old.

TABLE 2. *Radiographic features in 714 patients with pulmonary tuberculosis.*

Usual (multiple lesions) manifestations	No.	%*	Unusual (isolated lesion or normal) manifestations	No.	%*
Upper or multilobar lesions	616	86.3	Isolated lesion	81	11.4
Cavities with no fluid levels	529	74.1	Lower lobe opacities	38	5.3
Multilobar opacities	420	58.8	Lung mass(es)	10	1.4
Atelectasis	333	46.6	Cavities without lung opacities	5	0.7
Upper lobe opacities	196	27.4	Anterior segment of upper lobe opacity	4	0.6
Pleural thickening	108	15.1	Lingular opacities	4	0.6
Parenchymal calcification	57	8.0	Bilateral lower lobe opacities	4	0.6
Cavities with fluid levels	26	3.6	Pleural effusion	4	0.6
Pleural effusion	24	3.4	Pneumothorax	3	0.4
Hilar or mediastinal lymph node enlargement	21	2.9	Miliary distribution	3	0.4
Pneumo- or hydropneumothorax	15	2.1	Hilar or mediastinal lymph node enlargement	3	0.4
Total patients	620	86.8	Pneumomediastinum	2	0.3
			Middle lobe opacity	1	0.1
			Normal chest x-ray study	13	1.8
			Total patients	94	13.2

%*: Percentage is that of the total 714 patients.

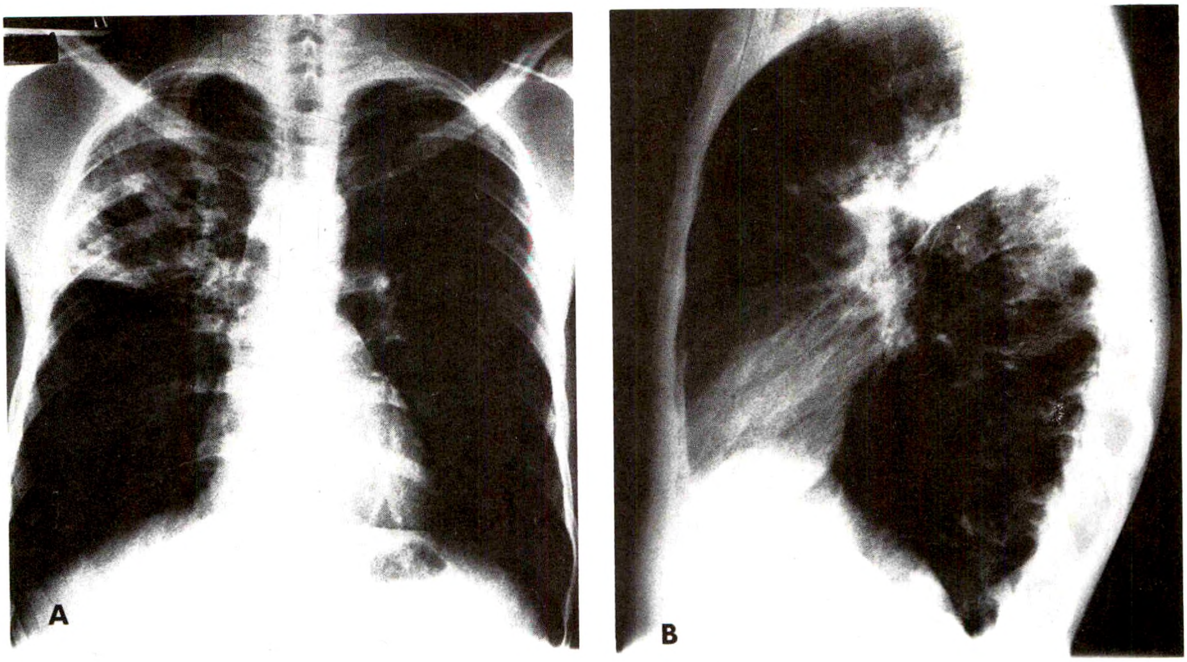

FIGURE 1. Posteroanterior (A) and lateral (B) views showing typical distribution of postprimary pulmonary tuberculosis. There is predilection for posterior segment of the right upper lobe. Note also the cavitation within the opacity.

Usual manifestations were seen in 86.8% (Figures 1,2) and unusual ones in 13.2% (Figure 3, Table 2). PTB mainly presented with upper or multilobar opacities (86.3%) with cavitation (77.7%) (Figure 4). The most common unusual radiographic manifestation was isolated lower lobe opacities, seen in 5.3% of the cases. Normal chest radiographs were seen in 1.8% of the cases.

Opacities involved more than one lobe simultaneously in 59.4% of the patients (Table 3). The right upper lobe was more frequently involved (18.9%) than the left upper lobe (10.5%). Of 12 patients younger than 15 years, ten had pulmonary opacities, one had isolated mediastinal glands, and one was normal. Multilobar involvement was also more common in this age group than in other age groups followed by left upper lobe involvement.

Several patterns of opacity were seen, and frequently more than one pattern in the same radiograph (Table 4). The most common predominating pattern was inhomogeneous (39.9%).

Cavities were seen in 78.4% of the patients, and were multilobar in 50.5% of these cases (Table 5). More cavities were seen in the right upper lobe (21.0%) than in the left upper lobe (12.6%). The site of cavitation showed no correlation with the site of consolidation. Five cavities with no obvious parenchymal opacities were categorized as unusual (Table 2).

Discussion

There was a significant male predominance in age groups above 15 years, which agrees with other observations [4]. Some investigators from developed countries have observed a shift in the age of presentation to above 40 years [5,6], but this was not seen in our study.

Most of our patients displayed the usual radiographic features of PTB. Extensive disease at presentation (i.e., multilobar involvement with cavitation) indicates that the disease had gone unrecognized or untreated [11].

Cavitation is very characteristic of PTB [12]. It rarely occurs at the time of primary infection but is secondary to the hyperimmune response to tuberculoprotein [13]. Cavitation customarily, but not always, indicates active infectious and extensive disease [11,12]. In our study the wall thickness of many cavities could not be estimated owing to the surrounding consolidation, but when this could be done, 13.5% had thick walls and 3.8% had thin walls. Although thick-walled cavities are more

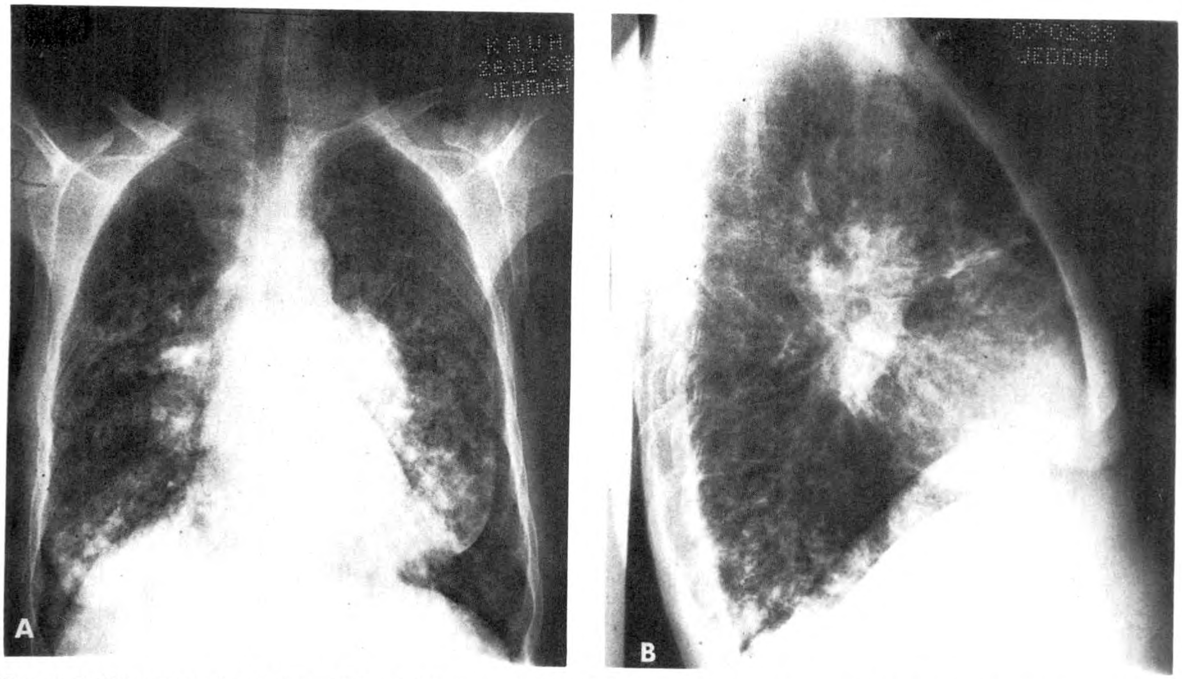

FIGURE 2. Posteroanterior (A) and lateral (B) views showing bilateral hilar lymph node enlargement and widespread lung opacities, mainly linear nodular and ill-defined.

TABLE 3. *Distribution of sites of lung opacities in 714 patients with pulmonary tuberculosis.*

Age group (yr)	RUL	RML	RLL	LUL	Ling.	LLL	Mul. Inv.	Total No.	Total %
0–14	1	–	1	3	–	–	5	10	1.4
15–29	60	–	11	42	2	4	174	293	41.0
30–44	56	1	8	23	2	7	160	257	36.0
45–80	18	–	5	7	–	2	85	117	16.4
Total	135	1	25	75	4	13	424	677	94.8

RUL = right upper lobe; RML = right middle lobe; RLL = right lower lobe; LUL = left upper lobe; Ling. = Lingular segment; LLL = left lower lobe; Mul. Inv. = multilobar involvement; % = percentage of the total of 714 patients.

likely to be active, histologically active cavities with a wall thickness of 1 mm or less have also been identified [14]. Air fluid levels were present in 3.6% cases that showed cavities in this study. The reported percentages vary as the following indicate: 20 to 60% [14], 21% [15], 67% [16], and seldom seen (no figure quoted) [13].

Associated atelectasis was seen in 46.6% of the cases. PTB is a well-known cause of obstructive as well as cicatrizing atelectasis [12]. Bronchial obstruction in PTB commonly results from peribronchial inflammation. Compression by enlarged lymph nodes and endobronchial granuloma is probably a less likely cause. Cicatrizing atelectasis is classically found in PTB and is the result of fibrosis

TABLE 4. *Frequency of different patterns of lung opacities.*

Pattern	Number	Percentage
Inhomogeneous	270	39.9
Acinar	204	30.1
Nodular (including 3 patients with miliary TB)	57	8.4
Homogeneous	46	6.8
Linear	26	3.8
Inhomogeneous/nodular	32	4.7
Reticulo/nodular	20	3.0
Ill-defined faint	10	1.5
Inhomogeneous/reticular	7	1.0
Inhomogeneous/linear	5	0.7
Total	677	100

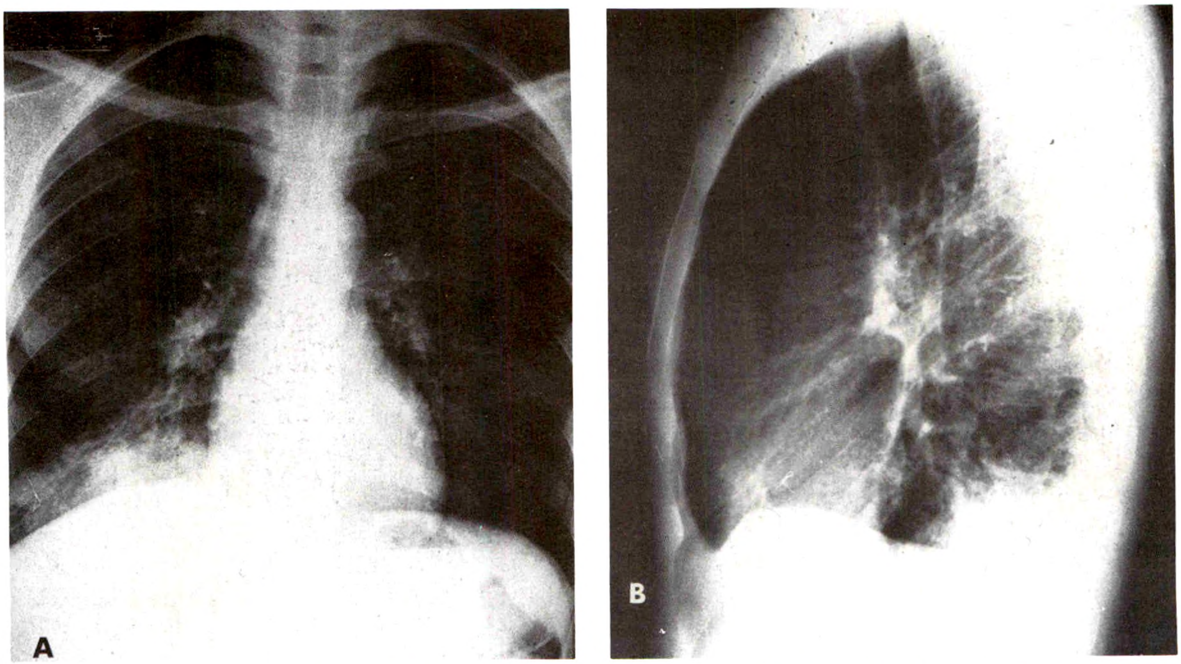

FIGURE 3. Posteroanterior (A) and lateral (B) views showing unusual pattern of pulmonary tuberculosis. The opacity is solely in the posterior and basal segments of the right lower lobe.

and scarring. It is similar to obstructive atelectasis but also displays coarse reticular densities and pleural thickening. These were not uncommon findings in the present study.

The radiographic pattern of opacities in PTB is often complex, with two or more patterns occurring in the same anatomic segment [1,4]. This was true in our study, with a predominating inhomogeneous pattern. Bronchopulmonary spread is often associated with an acinar pattern [13].

The presence of parenchymal calcifications, especially when coupled with a linear or nodular pattern, is often referred to as the fibrocalcific stage of the disease. It can be mistakingly regarded as "inactive" [1,13].

We encountered fewer unusual manifestations (13.2%) compared with other reports: 26.9% [4], 34% [5]. Such features can mask the true diagnosis and delay treatment. Many of the unusual manifestations may represent the primary form of the disease occurring in the adult population [17]. In the West, it is estimated that 10 to 20% of adult cases of PTB represent primary disease [5,17]. Pleural effusion is not as common in post-primary PTB as it is in primary disease [1,11], and is more commonly seen in adults than in children [13]. It can occur in more than 40% of the adult patients [1,17]. Pleural effusion may be an isolated finding

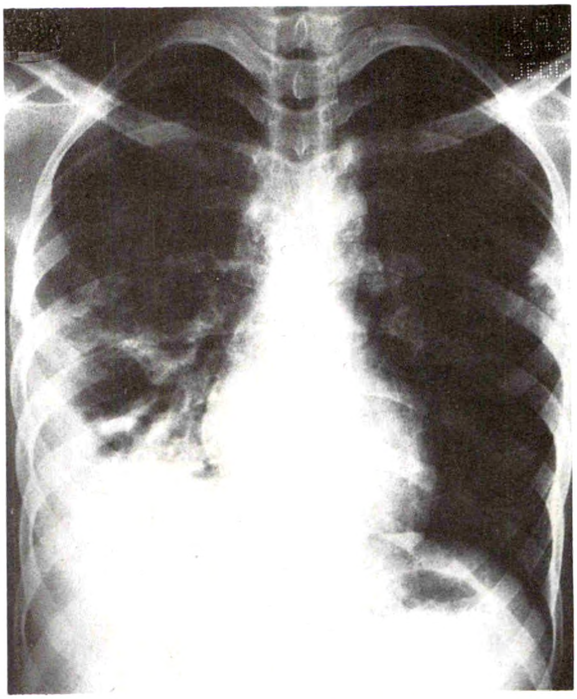

FIGURE 4. Posteroanterior view showing moderate-sized effusion associated with right lower lobe opacity and cavitation and left lower lobe opacity.

TABLE 5. *Distribution of sites of cavitary lung lesions in 714 patients with pulmonary tuberculosis.*

Age group (yr)	RUL	RML	RLL	LUL	Ling.	LLL	Mul Inv.	Total No.	Total %
0–14	1	–	–	2	–	1	2	6	0.8
15–29	59	–	8	44	2	4	119	236	33.1
30–44	68	1	5	32	2	8	106	222	31.1
45–80	22	–	4	12	–	2	56	96	13.4
Total	150	1	17	90	4	15	283	560	78.4

Mul. cav. = multilobar cavities; for other abbreviations, see Table 3.

in PTB (1.8%) [4], and was seen in 0.6% of our cases.

Isolated lower lobe tuberculosis is an unusual manifestation [4,6,8,18] and is probably seen more frequently in primary PTB [17]. Its reported incidence varies from 1 to 18.3% [4]. This compares favorably with our 5.3%. This form is often mistaken for viral or bacterial pneumonia [4]. It is considered to be more common in women and diabetics [6,13].

Pneumothorax is a well-described complication of PTB, and is thought to be due to rupture of tubercular cavities into the pleural space [8,11]. In our study, 0.3% of the patients had an isolated pneumothorax.

A normal chest radiograph does not exclude the existence of PTB [1], because the disease can occur in the proximal airway, it can be in an early miliary form, or there can be subradiographic pulmonary lesions [5,6]. One such patient in our series was a child below 15 years who returned a year later with obvious calcification in the right midzone. A strong clinical suspicion of PTB but with negative sputum findings and chest x-ray study warrants frequent clinical and radiological follow-up as well as sputum examination (e.g., every 2 to 3 months).

Masslike densities (or tuberculomatas) simulating bronchogenic carcinoma cause a diagnostic dilemma, particularly when uncalcified. They are a manifestation of primary as well as postprimary PTB [5,6,13,16].

Mediastinal and/or hilar lymphadenopathy was the sole manifestation of PTB in 0.4% of our patients. It is particularly associated with primary PTB in children [13]. Three of our 12 patients younger than 15 years had lymphadenopathy, but this incidence is low compared with the 65% reported in one study [3].

Many radiographic features of PTB are characteristic but not specific. Fungal, bacterial, other granulomatous, and even neoplastic diseases may stimulate PTB in its various forms [13]. Because PTB is far more common than all of those diseases combined in this part of the world [7], practitioners must recognize the various radiographic features of the disease and have a high index of suspicion whenever reading a chest radiograph. It is also worth noting that, although isolation of the causative organism is extremely important, this is not always possible [19], and this alone can seriously delay the institution of therapy.

The radiographic features of PTB as observed for Saudi Arabia do not differ significantly from those commonly described. However, the disease is usually extensive at presentation, making permanent lung damage inevitable. Recognition of the various radiographic manifestations, even in sputum-negative patients, would foster earlier management.

Acknowledgment

We thank Miss Yolanda Bacani for her assistance in typing this manuscript.

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CHILDHOOD IMMUNIZATION IN THE STATE OF QATAR: IMPLICATIONS FOR IMPROVING COVERAGE

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هناك ما يدل على نقص في استعمال خدمات تمنيع الأطفال في دولة قطر على الرغم من سهولة الحصول عليها. لذا فقد أجرينا دراسة استقصائية لتحديد حالة التلقيح وبشكل أهم، لمعرفة أسباب عدم القيام بالتمنيع الكافي لدى مجموعة مكونة من ٢٥٥ طفلاً في مرحلة ما قبل المدرسة يراجعون مراكز الرعاية الطبية الخارجية في مدينة الدوحة. وتم في هذه الدراسة استخدام استبيان للحصول على المعلومات اللازمة بما فيها المستوى التعليمي للوالدين. تبين لنا أن ٦٦٪ من الأطفال قد تلقوا جميع التمنيعات المحددة لأعمارهم وأن ١٢٪ تلقوا تمنيعاً جزئياً، و١٢٪ لم يتم تمنيعهم أبدا. تلقى ٨٨٪ من الأطفال الجرعة الأولى من اللقاح الثلاثي وشلل الأطفال (DPT/OPV) ، إلا أن ٥٧٪ فقط تلقوا الجرعة المعزِّزة الأولى عندما كان عمرهم ١٨ / / شهراً، وتلقى ٧٦٪ ثلاث جرعات من اللقاح الثلاثي وشلل الأطفال (DPT/OPV) . كانت الأسباب الرئيسية في حالات عدم التمنيع هي المعلومات المغلوطة وعدم دراية الوالدين بأهمية التلقيح بينما كانت الأسباب الرئيسية للتمنيع الجزئي هي سهو الوالدين والمعلومات المغلوطة والتأجيل بسبب طبي. وقد أظهرت الدراسة غلبة أمية الوالدين لدى الأطفال غير المنعين. ومن الأمور التي ستساعد بدرجة ملحوظة على زيادة نشر التمنيع في قطر، إنجاز حملة تثقيفية عامة نشطة ومستمرة بالإضافة إلى التطبيق الدقيق للبرنامج الموسع التابع لمنظمة الصحة العالمية حول سياسة التمنيع والذي يوصي بتقصي الحاجة إلى التلقيح لدى جميع الأطفال في كل فرصة تأتي بهم إلى مركز للرعاية الصحية. كما أن تأسيس نظام خاص لاستدعاء المتخلفين عن ذلك سيسهم في زيادة معدلات التمنيع.

In Qatar, there is evidence of underuse of the immunization services despite easy access to health care. We therefore undertook a prospective study to determine the vaccination status and, more importantly, the reasons for inadequate immunization of a group of 255 preschool children attending the outpatient care facilities in Doha. A questionnaire was used to obtain relevant information, including parents' educational background. Sixty-six percent of the children were fully immunized for their age group, 12% were partially immunized, and 12% were not immunized. Eighty-eight percent had received their first dose of DPT/OPV, but only 57% had received their first booster by 18 months of age; 76% had received three doses of DPT/OPV. The main reasons for nonimmunized status were misinformation and lack of awareness in parents about vaccination. Parental oversight, misinformation, and medical deferral were the main reasons for partial immunization. Parents of unimmunized children were often illiterate. In Qatar, establishment of an aggressive ongoing public education campaign, as well as strict implementation of the World Health Organization's Expanded Programme on Immunization's policy of screening all children at every health care contact for the need for vaccination, should substantially increase immunization coverage. Implementation of a recall system for defaulters should also lead to improved immunization rates.

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Presented in part at the VII Annual Meeting of the European Society for Paediatric Infectious Diseases, Lemmer, Holland, April 24, 1989.

The goal of immunization is to prevent disease both in individuals and in the community at large. Vaccination is the most cost-effective means of accomplishing this in childhood. The WHO, through its Expanded Programme on Immunization (EPI) and Health for All by the Year 2000 programme, has actively encouraged member countries to accelerate their immunization efforts and achieve high levels of coverage [1]. Despite some impressive advances, some three million children still die each year from vaccine-preventable diseases and another three million are permanently disabled [1,2].

In the state of Qatar, there is evidence of underuse of the immunization services [SO Foster, Centers for Disease Control, unpublished data, 1987], despite easy access to health care and a firm political commitment to the childhood vaccination program. To understand the reasons for this, we conducted a prospective study to determine both the vaccination status of a population of infants and young children attending pediatric and outpatient care facilities and the reasons for inadequate vaccination in some children. Our ultimate aim was to find ways of improving the immunization coverage in this country.

Material and Methods

Qatar has a total population of 370,000, two-thirds of whom live in the capital, Doha. It provides free health care through a nationwide network of 21 primary health care centers, each with a defined catchment area, and a large referral hospital that provides the only acute inpatient care in Qatar. The bulk of pediatric outpatient and emergency care for the country is in the capital at the outpatient facility of the Hamad Medical Corporation. Several other health care centers in the capital are also staffed with qualified pediatricians and tend to have large pediatric workloads. There is an excellent system of roads in Qatar, which connect all the towns with the capital, making health care easily accessible to all inhabitants.

Patient Population

Preschool children (aged 6 months to 4 years) seen at either the pediatric outpatient care facility of the Hamad Hospital or another major health center were entered into the study. Subjects were selected randomly during periods when authors (NK, BM, FE, RN, and MA) were scheduled for duty at the facilities. Parents were interviewed and patient history obtained by means of a questionnaire which sought information on educational background, the reason for attendance at the facility, and the immunization status of each child (i.e., fully immunized, partially immunized, or unimmunized, according to the recommended schedule). Immunization cards were inspected to verify the type of vaccines the child had received, and the dates of administration. If an immunization card was not available, verbal history was accepted after careful questioning. Knowledge, attitudes, and practices of parents concerning immunization were documented whenever a child was found to be unvaccinated or not up to date with the recommendations. Study subjects were enrolled over a two-year period between July 1987 and July 1989.

Vaccination Schedule

The current recommendations in Qatar are for BCG vaccination at birth, and DPT and OPV at 2, 4, and 6 months, with boosters at 18 months and at the time of school entry. Measles vaccination is recommended at 9 months and MMR at 15 months. BCG vaccination was not evaluated, as most deliveries in Qatar (more than 90%) occur in hospital where BCG is given routinely to all neonates [3].

Statistical Analysis

Statistical analysis was performed using chi-square analysis, and significance was defined as $P < 0.05$.

Results

Parents of 255 children completed the questionnaire. Vaccination cards were available for 45% (100/224) of the fully and partially immunized patients. A total of 88% (97/229) of the children were either partially or fully immunized for their age group (Figure 1). In the group of children aged 12 months or less, 35 of 46 (76%) were fully immunized. The immunization coverage for each vaccine is shown in Table 1. While 88% of all children had received their first dose of DPT/OPV, only 57% had received the booster dose at 18 months; 76% had received a total of three doses of DPT/OPV.

Misinformation and lack of awareness were the major reasons given by most parents (84%) for lack

TABLE 1. *Immunization coverage for each vaccine.*

Vaccine	Coverage (%)
DPT1/OPV1	88
DPT2/OPV2	82
DPT3/OPV3	76
DPT/OPV (booster)	57
Measles	73
MMR	71

TABLE 2. *Reasons given by parents for children being unimmunized.*

Reasons	No (%)
Vaccination thought to make child sick	9 (29)
Vaccination not considered necessary	9 (29)
No knowledge of vaccination program	8 (26)
Unable to get to vaccination center	4 (13)
Physicians postponed vaccination	1 (3)

TABLE 3. *Reasons for incomplete vaccination.*

Reasons	No. (%)
Parents forgot	14 (25)
Physicians postponed vaccination	7 (13)
Further vaccinations thought to make child sick	7 (13)
Did not think any further vaccination necessary	7 (13)
Family absent from country	6 (11)
Transport problems	5 (9)
Delayed by parents because child was sick	4 (7)
Problems getting to clinic on appointed day	3 (5)
No reason given	3 (5)

of immunization in their children (Table 2). Unrealistic fears regarding vaccine side-effects were also prevalent. Some parents considered immunization a futile exercise, as they believed their child's health and well-being were in God's hands.

Parental oversight or misinformation and medical deferral were the main reasons (64%) for partial immunization in children (Table 3). Some parents expressed extreme frustration at their child being refused vaccination because of a mild intercurrent illness.

The relationship between the education level of parents and vaccination in their children is shown in Figure 2. Unimmunized children were more likely to have illiterate parents: 46 of 62 parents (74%) of unimmunized children were illiterate compared with 83 of 336 parents (25%) of fully immunized children (chi-square, $P < 0.001$).

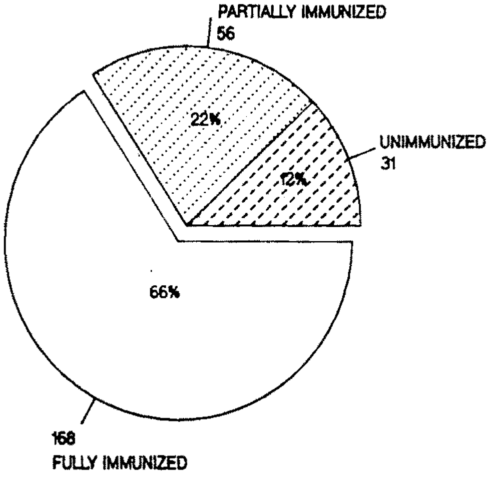

FIGURE 1. Immunization status of children enrolled in the study.

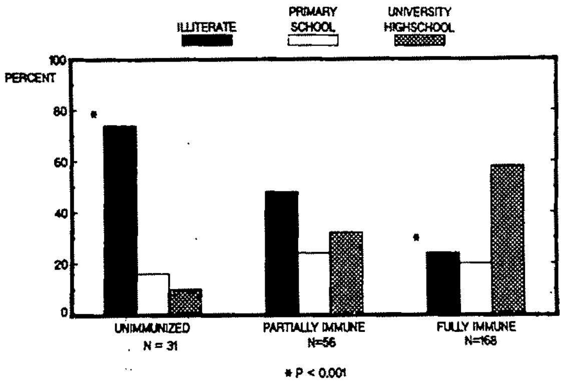

FIGURE 2. Educational level of parents and children's immunization status.

Discussion

Our findings suggest there is need for improvement in Qatar's vaccination program. While the sampling technique used in our study did not conform to the "cluster sampling methods" used by the WHO [4], we feel our results are still representative for the population because of the wide referral areas served by our health facilities.

One of the measures of progress for the EPI is immunization coverage of children before their first birthday [5]. That 76% of the infants (aged less than 12 months) were fully immunized suggests a recent and modest improvement in vaccination in Qatar, as most infants were recruited during the latter part of the study.

The lowest vaccine coverage was seen for the booster dose of DPT/OPV, which is given at 18 months of age. Coverage with successive DPT/OPV vaccinations progressively decreased. This drop-out rate is probably related to health services not setting up systems for following and identifying eligible vaccinees [6]. Evidence suggests that an immunization program coordinated by a computer-controlled system, which rapidly identifies unimmunized individuals and defaulters, results in a higher rate of immunization [7].

Vaccination cards were available for only half of the fully and partially immunized children. Despite this, studies from Sudan have shown that verbal information obtained from mothers tends to be accurate, and does not lead to overestimates of immunization rates [8].

In our study, the main reasons for inadequate immunization were a basic lack of information and awareness in parents and the difficult logistics of vaccine delivery. Illiteracy in parents was significantly associated with noncompliance with childhood vaccination requirements. These findings resemble those observed in immunization surveys from other developing countries [9,10]. Conversely, low immunization rates observed in some Western countries are probably due to declining incidences of target diseases with consequental professional apathy, as well as to an increasing awareness of the potential, but very rare, risks of vaccination [2,11]. Thus immunization is frequently deferred for a variety of "mythical contraindications" [12].

To improve vaccination rates in Qatar, the accent should first be on an aggressive and ongoing public education campaign, thereby creating consumer demand for vaccination [11]. The community needs to be given relevant and accurate information on the risks and benefits of immunization, and its importance. Illiteracy must also be eradicated. National and community leaders need to be actively involved in the immunization program. Health workers should also be instructed in ongoing training programs that foster a high degree of commitment and motivation.

Information systems should be established to identify eligible vaccinees and defaulters. Alternatively, outreach programs could be established that provide vaccination services to individual defaulters in the community, or to areas with poor immunization rates [2]; these could be held at prearranged times and sites, and at the convenience of the community. A successful defaulter retrieval system has been operating in the Sultanate of Oman for some time. Despite the lack of exact postal addresses and a large nomadic population (as in Qatar), defaulters are located through tribal connections, usually through their sheikh [P Malankar, personal communication].

The EPI policy of determining every child's immunization status at every contact with health services should be actively promoted. Opportunities for immunization are often missed if children are seen for reasons other than preventive care [13]. Low-grade fever, mild upper respiratory tract infections, and diarrhea should not contraindicate immunization [2]. Screening by hospital pediatric staff is especially needed so that inadequately immunized and hospitalized children are identified and vaccinated on discharge.

Immunization coverage should increase substantially in the country if the preceding recommendations are adopted. The elimination of EPI's target diseases in Qatar seems tantalizingly close to being achieved.

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TRAUMATIC ASEPTIC OSTEITIS PUBIS

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أجرينا دراسة لثمان وسبعين من حالات التهاب عظم العانة الرضحي العقيم لدى رياضيين سعوديين لتوضيح الملامح السريرية والشعاعية لهذه الحالة، وكذلك لتحديد أسبابها ومعرفة نتائج علاجها. كانت أكثر الشكاوى تواردا لدى المرضى : ألم في الأربية وأسفل البطن وإيلام فوق منطقة الارتفاق العاني. وكانت أكثر التغيرات الشعاعية تواترا توسع العظم وانحلاله في منطقة الارتفاق العاني. ولم تظهر الفحوص المخبرية الروتينية أي شذوذ لدى أي من مرضانا. وقد أدى العلاج بالطريقة المحافظة والتي تشتمل على تجنب النشاطات الرياضية واستخدام مضادات الالتهاب غير الستيرويدية والعلاج الطبيعي إلى شفاء ٧٥٪ من مرضانا. أما باقي المرضى ونسبتهم ٢٥٪ فقد احتاجوا إلى مزيد من العلاج. إن هذا الاضطراب شائع نسبيا بين لاعبي كرة القدم السعوديين. وهو ناجم على الأرجح عن الإصابات الرضحية. وهكذا يتبين لنا نجاح الطريقة المحافظة في العلاج لدى معظم المرضى.

We studied 78 cases of traumatic aseptic osteitis pubis among Saudi athletes to elucidate the clinical and radiological features of the condition as well as the outcome of management and the etiology. The most common presenting complaints were pain in the groin and lower abdomen, and tenderness over the symphysis pubis. Widening and osteolysis of the symphysis pubis were the most frequent radiological changes. Routine laboratory tests showed no abnormalities in any of our patients. Conservative treatment, consisting of avoidance of sporting activity, use of nonsteroidal antiinflammatory drugs, and physiotherapy, effected cure in 75% of our patients. Further management was needed in the remaining 25%. The disorder is relatively common among Saudi football players, with trauma the likely cause. Conservative treatment is successful in most patients.

Traumatic aseptic osteitis pubis, also known as osteitis pubis [1], pubic symphasitis [2], osteochondritis of the symphysis pubis [3], adductor avulsion injuries [4], adductor tendinitis and musculus rectus abdominis tendopathy [5], and the gracilis syndrome [6], is a painful disorder involving the symphysis pubis, but with an uncertain etiology. Beer [7], in 1924, reported infection of the symphysis pubis following operation, and this represents probably the first report of the disorder. Since then, many causes have been suggested. These include aseptic necrosis [8], chronic low-grade infection [9], trauma [10], microtrauma causing thrombosis and aseptic necrosis of the bone and cartilage secondary to the "end artery" arrangement [1], and subacute periostitis [11,12].

Trauma is most accepted as the cause, and the mechanism of injury to the symphysis pubis is postulated as stress on the joint exerted by the gracilis-adductor group of muscles adducting the pelvis against a foot that is relatively fixed in external rotation [13–15].

The condition is common in soccer players and race walkers, and is also seen in runners who abruptly increase their mileage or add interval training with speed work [16]. Other sports in which this disorder is seen include rugby, wrestling, ice hockey, cycling, and cricket [17].

The presenting complaint usually consists of pain related to the abdomen, leg, hip, or groin and occasionally localized to the symphysis [13,17].

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Accepted for publication 30 May 1990.

Onset may be sudden or insideous [17]. There may be tenderness on palpation of the symphysis and pain provoked by adduction of the limb against resistance or with extreme passive abduction [13,16,17]. Radiological findings include: no abnormality, loss of bone definition, widening of the symphysis, erosions, sclerosis, a mixed pattern of bony destruction and sclerosis, periosteal reaction, and hypertrophic changes with asymmetry [13,14,16–18].

The clinical and radiological differential diagnosis include: inguinal hernia, prostatitis, orchitis, urolithiasis, muscle strain, osteomyelitis, ankylosing spondylitis, stress fracture, Reiter's syndrome, hyperparathyroidism, infection, and primary and secondary tumors [16,17,19]. Treatment consists primarily of rest, antiinflammatory drugs, and stretching exercises [13,16,17,20]. Occasionally local infiltration with steroids may be beneficial [5,13], especially if conservative treatment fails and the patient is unwilling to change or abandon his sporting activity. Adductor tenotomy and/or a rectus abdominis tenotomy may be indicated in some patients [5].

We present the clinical and radiological features of this condition, along with the outcome of management, and discuss the possible causes.

Patients and Methods

Of the total number of sports-related injuries seen at the Sports Medicine Hospital during 1988, traumatic aseptic osteitis pubis was diagnosed in 78 patients. These patients were treated and followed up for a minimum of 18 months, and form the basis of this study. The following data were recorded for each patient: age, sex, pain, duration of symptoms, clinical findings, radiological findings, laboratory results, treatment, and outcome.

Clinical assessment included the site of tenderness on palpation, the range of passive and active motion, and the presence of pain on passive abduction and active adduction against resistance.

Radiological examination included the standard anteroposterior x-ray study of the pelvis and hip, as well as an anteroposterior coned view of the symphysis pubis. As a control, we examined the pelvic x-ray studies of 25 football players who were seen for reasons not related to this condition. When instability was suspected, a coned view of the symphysis pubis was taken standing on one limb at a time–"flamingo view" [16]. A difference of more than 2 mm in the level of symphysis pubis was considered diagnostic of instability at the symphysis pubis. A technetium isotope bone scan was done on a small number of patients.

The laboratory studies were uniform for all patients and included: complete blood count, sedimentation rate, serum calcium, inorganic phosphate, and urinalysis.

The initial treatment for all patients was conservative and consisted of avoiding sporting activity for 4 to 6 weeks, nonsteroidal antiinflammatory drugs, and physiotherapy. Following this, a program of muscle stretching was instituted. If this approach failed, local injection of steroids was done and/or the patients were advised to change, modify, or abandon their sporting activity. None of our patients underwent surgical intervention. The condition was considered cured if the patient was asymptomatic after resuming his usual sports activity.

Results

There was an 8.8% prevalence of traumatic aseptic osteitis pubis among Saudi athletes treated for sports-related injuries at the Sports Medicine Hospital in the year 1988.

All 78 patients were male (age range, 18–31 years; average, 22 years).

Most (90%) were football players, and the remainder participated in handball (4%), karate or some other martial art (4%), and other sports (2%).

All patients complained of pain: 42% had pain in the left groin, 15% in the right groin, 18% in both groins, and 25% in the lower abdomen and symphysis pubis. There was a negative history of obvious trauma in 65% of the patients for whom onset of symptoms was gradual. There was a definite history of trauma in 35%, with a sudden onset of symptoms. Average duration of symptoms at presentation was 3 months.

On palpation, 92% of the patients had tenderness around the symphysis pubis with or without tenderness in the groin; only 8% had tenderness in the groin per se. Passive abduction and active adduction against resistance provoked pain in 70% of the patients.

The standard radiological examination (i.e., anteroposterior pelvis and coned view of the symphysis pubis) showed no abnormality in 17% of the cases, osteolysis and widening of the symphysis in 75% (Figure 1), and a mixed pattern of osteolysis and sclerosis in 8%. The changes were asymmetrical in 80% and symmetrical in 20%. None of the x-ray studies for control subjects showed any abnormal radiological changes in the symphysis pubis. A flamingo view showed instability in 15% of the cases (Figure 2). A technetium isotope bone scan was done in 12 patients, and the scan showed increased activity in the symphysis pubis in 11.

Conservative treatment effected cure in 75% of the patients. Failure of conservative treatment and recurrence occurred in 25%. These patients were advised to change and/or abandon their sports activity. None of our patients underwent surgical intervention.

Discussion

The cause of osteitis pubis in athletes remains uncertain, and this may explain the maze of terms applied to the disorder. We believe like many others that trauma is the most likely cause and have found no clinical or laboratory evidence to suggest infection. Biopsy of the lesion has shown only a nonspecific inflammation with a mononuclear cell infiltrate, bone resorption, and fibrous tissue replacement of the symphysis of the fibrocartilage [21].

The trauma can be obvious and lead to the sudden onset of symptoms as was the case in 35% of our patients, or it can be a subtle process that leads to the gradual onset of symptoms. This was seen in 65% of our patients. We believe the latter arises from excessive or repetitive stress inflicted on the symphysis pubis.

The clinical, radiological, and laboratory findings in our study are similar to those observed by others [13,14,16–18]. Pain in the groin and/or symphysis pubis and lower abdomen was the main presenting complaint in our patients. Tenderness over the symphysis pubis, with or without groin tenderness, was encountered in 92% of the cases, and such a clinical presentation makes the diagnosis highly suggestive.

Normal laboratory results and the characteristic x-ray findings of widening and osteolysis of the symphysis pubis, as was seen seen in 75% of the patients, all confirm the diagnosis. The changes were asymmetrical in 80% of the cases.

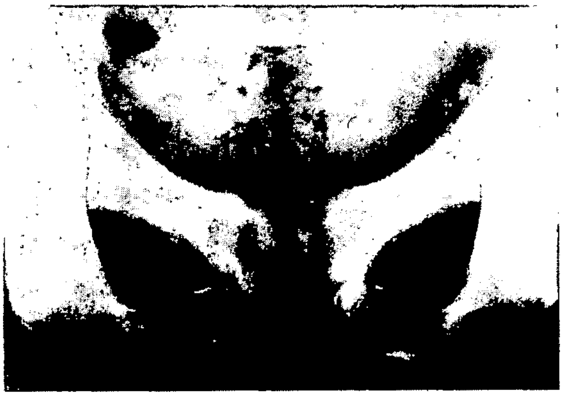

FIGURE 1. X-ray study showing osteolysis of the symphysis pubis.

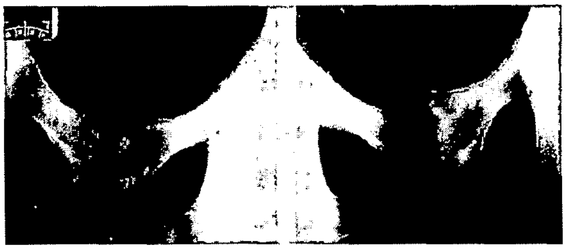

FIGURE 2. X-ray study (flamingo view) showing instability of the symphysis pubis.

Patients who lacked radiological changes were mostly those whose symptoms had lasted for less than 1 month. Though one may question the diagnosis in this group, we believe treatment should be based on the clinical findings. If confirmation of the diagnosis is needed, a technetium bone scan may help.

Most authors regard the radiological changes as part of this disorder [13,14,16–18]. Martens et al [5] considered the radiological changes of the pubis symphysis nondiagnostic, as soccer players with no history or complaint of groin problems often exhibit these changes. We could not find any such abnormal radiological changes in a control group of 25 pelvic x-ray studies of soccer players who were seen for reasons not related to this disorder. Accordingly, we consider the radiological changes a manifestation of the disorder.

Most practitioners agree that the preliminary form of treatment should be conservative. This approach is well known and documented in the literature [3,16,17,20] and includes avoidance of sports activity for 4 to 6 weeks, a course of nonsteroidal antiinflammatory drugs, and physiotherapy.

We adopted this approach initially in all our patients, and the cure rate was 75%. Recurrence and/or persistence of symptoms occurred in 25%. Those patients who did not respond to conservative methods were advised to modify and/or abandon their sporting activity. Those who followed this advice showed improvement and became gradually asymptomatic.

In view of the confusion among physicians regarding this disorder, we suggest the use of a specific name that represents the cause as well as the clinical and radiological manifestations. With this in mind we recommend the term *traumatic aseptic osteitis pubis.*

Acknowledgment

We thank HRH Prince Faisal Bin Fahad Bin Abdul Aziz, President of the General Presidency of Youth Welfare for his help, support and encouragement.

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SURGICAL AUDIT: A PROSPECTIVE STUDY OF THE MORBIDITY AND MORTALITY OF ACUTE APPENDICITIS

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تم تشخيص التهاب الزائدة الحاد سريريا في ٣١٧ مريضا بين شهري مارس وسبتمبر من عام ١٩٨٩م، درسنا هذه المجموعة كجزء من مراجعة استطلاعية، خططت الدراسة لتحديد دقة التشخيص، ومقارنة المظهر العياني للزائدة عند العملية، وتقارير التشريح النسجي المرضى اللاحقة والمضاعفات المتعلقة بالمراضة والوفيات المصاحبة لاستئصال الزائدة في الحالات الطارئة. تأكدت صحة التشخيص السريري في ٢٧٨ مريضا (٨٨٪). جاءت نتيجة فتح البطن الاستقصائي سلبية في تسعة وثلاثين (١٢٪) من هؤلاء المرضى. ولم تحدث وفيات ولكن خمج الجرح كان السبب الأساسي لزيادة المراضة في سبعة وثلاثين (١٢٪) من المرضى. وحدثت أعلى نسبة من الخمج الجرحي بين المرضى الذين تكوّن القيح لديهم في الصفاق (٢٠٪)، أو الذين أصيبوا بالتهاب الزائدة الثاقب أو المواتي (٢٥٪). ولدى مقارنة المظهر العياني للزائدة مع نتائج التشريح النسجي المرضى اللاحقة تبين وجود خطأ إيجابي كاذب بنسبة ٧٪ وخطأ سلبي كاذب بنسبة ٤٢٪. يجب ملاحظة مظهر الزائدة جيدا أثناء استئصالها بحيث يمكن استكمال الأسلوب الجراحي الفني الدقيق بمعالجة وقائية مناسبة بالمضادات الحيوية لتفادي خمج الجرح، والبدء بذلك وقت إجراء العملية.

Between March and September 1989, acute appendicitis was clinically diagnosed in 317 patients who were studied as part of a prospective surgical audit. The study was designed to determine the accuracy of diagnosis, comparison of the macroscopic appearance of the appendix at operation, and subsequent histopathology and complications associated with the morbidity and mortality of emergency appendectomy. The clinical diagnosis was correct in 278 patients (88%). Thirty-nine (12%) of the patients had a negative laparotomy. There was no mortality, and wound infection was the source of increased morbidity in 37 (12%) patients. The highest incidence of wound infection was among those who had pus in the peritoneum (20%) or had a perforated or gangrenous appendix (25%). When the macroscopic appearance of the appendix was compared with the subsequent histopathological findings, a false positive error of 7% and a false negative error of 42% was found. During appendectomy the gross appearance of the appendix must be carefully noted so that a meticulous surgical technique can be complemented by appropriate antibiotic prophylaxis against wound infection, started at the time of surgery.

Wound infection is the most common source of postoperative morbidity following emergency appendectomy. The morbidity and mortality associated with appendicitis is further increased when perforation or gangrene occurs. This prospective study was designed to audit the morbidity and mortality of acute appendicitis and to determine the measures that can prevent wound infection after appendectomy. The most important observation during appendectomy is the macroscopic appearance of the appendix. Comparison of the macroscopic appearance at operation with subsequent histopathological findings has shown a

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Accepted for publication 30 May 1990.

false positive rate of 6.9 to 14.5% and a false negative rate of up to 10.3% [1,2]. If a perforated or gangrenous appendix is observed, or pus is found in the peritoneal cavity, the surgeon can then modify the intraoperative management in order to diminish the risk of wound infection in such patients.

Patients and Methods

All patients over the age of 12 years undergoing emergency appendectomy at Asir Central Hospital from March to September 1989 were included in this study. A questionnaire was devised that was completed at the time of admission, operation, discharge, and one-month follow-up. It recorded the surgeon's opinion of the macroscopic appearance of the appendix, and whether there was pus in the peritoneal cavity and whether a pursestring suture was applied. We checked the accuracy of the clinical diagnosis of acute appendicitis against the surgeon's description of the gross appearance at operation and subsequent histopathological findings of the appendix. Antibiotics were not routinely used. Wound infection was defined as discharge of pus or positive bacteriological culture from a wound discharge [3]. When wound infection was suspected, swabs were taken from aerobic and anaerobic culture. All patients were followed up for one month after operation, as wound infection can occur late after the discharge of patients from hospital [4].

Results

This study included 317 patients (200 males, 117 females; 1.7:1) who underwent emergency appendectomy. Of these patients, 297 (93.7%) were below the age of forty. Only nine patients (2.8%) were aged fifty or above (Figure 1). The most frequently occurring age (mode) was 20 years. Age range was 13 to 70 years. Wound infection developed in 37 patients (12%). When this occurred during the first admission or was the reason for readmission, a mean hospital stay of 9.5 days was noted, as compared with 4.3 days for patients who did not suffer wound infection (Table 1). The highest incidence of wound infection occurred in patients who either had pus in the peritoneum (20%) or had a perforated or gangrenous appendix (25%) (Table 2).

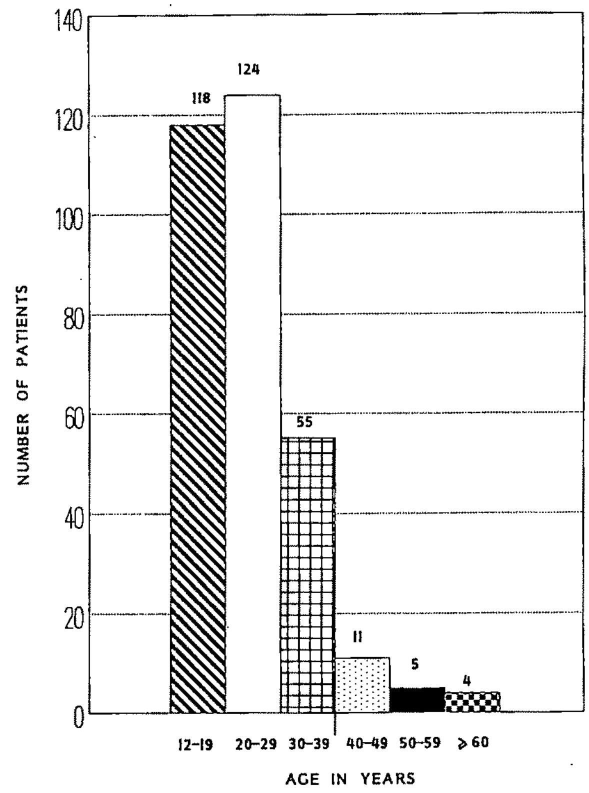

FIGURE 1. Age distribution of patients.

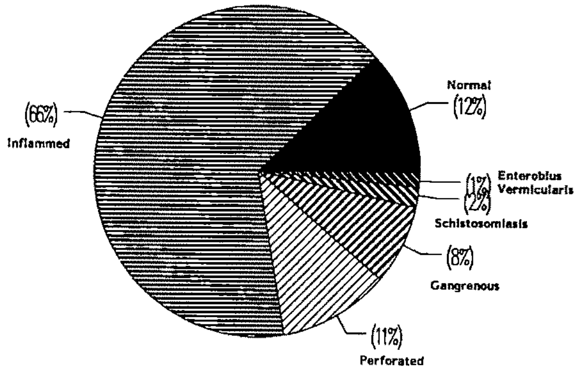

FIGURE 2. Histological findings of the appendix.

TABLE 1. *Postoperative hospital stay (days).*

	All patients (N = 317)	Patients with wound infections (N = 37)
Mean	4.3	9.5
Range	2–22	7–22
Median	4	8.5
Interquartile range	3–5	8–11

TABLE 2. *Wound infection (%).*

	No.(%)
All patients (N = 317)	37 (12)
Normal appendix (N = 39)	3 (8)
Inflamed appendix without perforation or gangrene (N = 218)	19 (9)
Perforated and gangrenous appendix (N = 60)	15 (25)
Pus in the peritoneum (N = 102)	20 (20)

TABLE 3. *Wound infection: pursestring versus no pursestring suture.*

Group	Perforated gangrenous (%)	Wound infection (%)	Mean hospital stay (days)
Pursestring (N = 242)	53 (22)	25 (10)	4.2
No pursestring (N = 75)	24 (32)	12 (16)	4.4

There was a higher representation (32%) of patients with perforated or gangrenous appendix whose appendectomy had not included a pursestring suture, and once these patients were excluded, there was no difference in the incidence of wound infection between the pursestring and no pursestring groups (Table 3).

In 39 patients (17 males, 22 females), the appendix was reported to be histologically normal, yielding a negative laparotomy rate of 12%. This includes five females whose laparotomy was indicated due to twisted right ovarian cyst, pyosalpinx (two patients), bleeding from ovary due to ruptured ovarian follicle, and ruptured ovarian cyst, all producing features of local peritonitis of the right iliac fossa (Figure 2).

At operation, 284 appendices were considered inflamed (89.6%), but only 264 (83.3%) showed histological evidence of acute inflammation. This gives a false positive error of 7%. Macroscopically, 33 appendices were considered normal but only 19 were histologically normal (58%), yielding a false negative error of 42%. Description of the gross appearance of the appendix by the surgeon was correct for 89.3% of the patients.

Discussion

Wound infection is the most common source of postoperative morbidity following emergency appendectomy. Patients with an inflamed appendix without peritoneal contamination, perforation, or gangrene had a 9% rate of wound infection. A similar wound infection rate (8%) was observed when a normal appendix was removed, but this rate increased to 25% when a perforated or gangrenous appendix was found (see Table 2). Similarly, we have observed a 20% incidence of wound sepsis when pus was found in the peritoneal cavity. Delay in diagnosis has been proposed as contributing to the increased frequency of postoperative wound infection [5–7], but this is not confirmed [6], because the progression of acute appendicitis is probably variable and does not follow the relentless course from intramural inflammation to luminal obstruction, perforation, or gangrene. A variety of host defenses may operate in resolving the process prior to accurate diagnosis. However, the degree of operative contamination of the wound is one of the most important risk factors for postoperative wound sepsis following appendectomy. In such high-risk patients, prophylactic use of antibiotics started before or during surgery has been shown to produce an acceptably low wound infection rate [8,9]. A careful technique aimed at reducing operative contamination of the wound and effective prophylactic antibiotics suitable against both aerobic and anaerobic organisms started at the time of surgery may help to reduce the high incidence of wound sepsis in this group of patients. This observation forms the basis of our future prospective randomized trial.

This study shows a high incidence of acute appendicitis occurring in subjects between the ages of 12 and 29 years (76.3%). After age of 40 the incidence decreases to 6.3%. This increased incidence may be explained by Baker's "hygiene hypothesis" [10] which points to improvements in sewage disposal and drinking water supplies that have reduced the exposure of infants and children to enteric organisms, thus altering the response of adolescents to bacterial and viral infections triggering acute appendicitis. Clearly the absence of enteric infections in infancy and presence of infection in adolescence could play a part in this increased incidence of acute appendicitis.

Avoidance of a pursestring suture did not increase the morbidity. When used in patients to invaginate the stump, their hospital stay and rate of wound sepsis did not alter. We suggest that the omission of inversion of the ligated appendix stump simplifies the appendectomy without any increase in morbidity. A similar conclusion was reported by Watters and Engstrom [11,12].

The correlation between the gross appearance of the appendix at appendectomy and subsequent histological examination showed that surgeons correctly reported gross findings in 89.3% of the patients. They incorrectly reported gross findings in 10.7% of the patients. Surgeons, who were mostly of registrar status, were often wrong when they deemed the gross appearance as normal. Their false negative rate was 42%. When terms like "mild," "early," "slight," or "minimal" inflammation of the appendix are used, a false positive group with an error of up to 80% has been identified [2]. We suggest that surgeons should define the gross appearance of the appendix in terms of "normal," "inflamed," "perforated," or "gangrenous." This would minimize the false positive rate, as in the present study, to about 7%. There was a 12% incidence of negative laparotomy. Irvin [13] reported a 16% incidence of unnecessary appendectomies chiefly due to misdiagnosis in patients suffering from nonspecific abdominal pain.

Clearly the most important observation to make at appendectomy is whether the appendix is perforated or gangrenous and if pus is present in the peritoneal cavity. Such observations will direct the operative technique toward reducing wound contamination by a meticulous approach and the peroperative use of antibiotics to reduce the morbidity of acute appendicitis.

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LIMITING THE USAGE OF BLOOD PRODUCTS IN CARDIOVASCULAR SURGERY

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درسنا تأثير تطبيق برنامج ذي خمسة أجزاء هدفه الاقتصاد في صرف مشتقات الدم على استهلاك منتوجات الدم من قبل مرضى أجريت لهم جراحة قلبية وعائية رئيسية . شجعنا الأطباء والممرضات على التقيد بمجموعة من الإرشادات الهادفة إلى تقليل تعرض هؤلاء المرضى للمضاعفات المرتبطة بنقل منتوجات الدم إليهم . وأمكن، من خلال هذه الجهود، خفض الكميات المستعملة من الخلايا الحمراء المركزة والمصورة الطازجة المجمدة والصفيحات والراسب القري بدرجة ملحوظة . وقد انخفض إجمالي استعمال منتوجات الدم، بعد بدء برنامج الاقتصاد، بنسبة ٢٩٪ بالرغم من زيادة قدرها ٤٦٪ في عدد الحالات الجراحية كما حدث انخفاض بنسبة ٥٣٪ في مقدار التعرض للمتبرعين (الوحدات المنقولة من منتوجات الدم) لكل مريض .

We studied the effect of the initiation of a five part program of blood component conservation on blood product utilization in patients undergoing major cardiovascular surgery. We encouraged physicians and nurses to adhere to a set of guidelines that would limit the exposure of these patients to complications associated with blood product administration. Through this effort the amounts of packed red cells, fresh frozen plasma, platelets, and cryoprecipitate used were markedly reduced. After the start of the conservation program, overall blood product usage was reduced 29% despite a 46% increase in the surgical caseload, and there was a 53% decrease in the amount of donor exposure (units of individual blood products administered) per patient.

Modern transfusion practice in cardiac surgery is directed toward keeping the number of administered blood bank products to a minimum. In some hospitals, over 90% of patients undergoing coronary artery bypass grafting (CABG) do not receive any blood products as part of a comprehensive blood conservation program [1]. We recently reevaluated our use of blood products and embarked on a program to reduce the amount of patient exposure to infectious agents such as HIV-1 and hepatitis viruses. This effort was based on the following maneuvers whenever possible: removal of 450 to 900 ml of the patient's blood prior to cardiopulmonary bypass with reinfusion after reversal of heparinization; reinfusion of all possible blood from the oxygenator at the conclusion of bypass; withholding the prophylactic administration of fresh frozen plasma (FFP), platelets, and cryoprecipitate until laboratory tests indicated specific coagulation deficits; acceptance of postoperative normovolemic anemia (hematocrit, 25–30%); and reinfusion of postoperative mediastinal drainage. We report here the results of a concerted effort in the operating room and ICU to use less blood products in patients undergoing a variety of cardiac surgical operations.

Methods

We studied the blood product utilization of all patients at our hospital who were undergoing CABG, single valve replacement or repair, multiple valve operations, reoperations for valve repair

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Accepted for publication 30 May 1990.

or replacement, closure of atrial septal defect in patients above and below 16 years of age, and ventriculoseptal defect closure. All patients undergoing these operations from February 1 to August 31, 1988, were placed in the control group (Group I). A second group of patients operated on from May 1 to October 31, 1989 (Group II), was studied after the introduction of a new set of procedures and guidelines governing blood product administration.

The following conservation techniques were utilized whenever possible for the patients in Group II:

1. Withdrawal of 450 to 900 ml of the patient's blood from the sideport of an 8.5 F percutaneous sheath introducer kit (Arrow AK 09801) after insertion of the Swan-Ganz catheter or from a 16ga × 8-inch central venous catheter, both inserted through an internal jugular or subclavian vein. Blood was collected by gravity into a bag containing 63 ml of citrate phosphate dextrose adenine solution (CPDA-1) over a period of 5 to 10 minutes for each 450 ml. This autologous blood was reinfused after neutralization of heparin. Prebypass blood withdrawal was not used when the patient's weight was less than 60 kg or the hemoglobin was less than 110 gm/L.
2. Reinfusion of all possible blood from the pump oxygenator after discontinuation of bypass, either through the aortic cannula or by intravenous infusion.
3. Acceptance of normovolemic anemia in patients who were not actively bleeding before the transfusion of packed cells.
4. Reinfusion of mediastinal chest tube drainage in the ICU using a described technique [2].
5. Administration of platelets, cryoprecipitate, and fresh frozen plasma only after specific coagulation deficiences could be demonstrated by coagulation tests. If the patient was not actively bleeding postoperatively, transfusions of platelets were withheld for platelet counts over 80,000; cryoprecipitate was given if the fibrinogen level was less than 1.0 gm/L; and FFP was reserved for patients with elevated prothrombin time (PT), partial thromboplastin time (PTT), thrombin time, and reptilase time.

All of these conservation methods represent a significant departure from our previous transfusion practice [3], which was used by Group I.

All patients in both groups were anesthetized with fentanyl (50 μg/kg) or sufentanil (5–10 μg/kg) supplemented with isoflurane or additional narcotics. Patients were anticoagulated with 300 units/kg of heparin before initiation of cardiopulmonary bypass. Adequate heparinization was assured by giving additional heparin to maintain the activated coagulation time (ACT) above 480 seconds. A disposable membrane oxygenator with a crystalloid prime was employed and bypass was carried out at 24 to 28°C. Cold potassium cardioplegic ischemic arrest was used in all cases.

At the conclusion of bypass, heparin was neutralized with protamine sulfate 1.5 times the initial heparin dose. Additional protamine was given if the ACT did not return to baseline levels. Platelet count and fibrinogen levels were monitored during bypass and the following tests were performed when the patient arrived in the ICU: hemoglobin, hematocrit, fibrinogen, PT, PTT, thrombin time, reptilase time, and fibrin degradation products. Transfusion of packed cells, platelets, cryoprecipitate, and FFP was recorded as units per patient, and accurate records of blood product usage were kept by the blood bank for each patient. Efforts were made to follow these blood product conservation guidelines for each patient during surgery and in the postoperative period. Whenever possible, the administration of blood products was discussed at daily morning rounds in the ICU. Transfusions were deemed inappropriate if they were not justified by the results of hemoglobin levels and coagulation tests.

Data were analyzed using a Student's two-sample *t* test.

Results

There were 177 patients in Group I and 259 in Group II. The number of patients undergoing the different surgical procedures is shown in Table 1. No significant differences in the height, weight, preoperative hemoglobin level, or mortality were found between Group I and Group II patients for each type of operation. The amounts of blood products utilized for the two patient groups are shown in Table 2 and demonstrate reduced blood product usage in Group II patients for all four types of blood products. These results were statistically significant ($P < 0.001$). In addition,

TABLE 1. *Summary of patients according to surgical procedures.*

Procedures	No. of patients 1988	No. of patients 1989
CABG	44	66
Single valves	50	81
Multiple valves	24	25
Redo	13	22
ASD > 16 years	16	20
ASD < 16 years	11	17
VSD	19	28
Total	177	259

CABC = coronary artery bypass graft; ASD = atrial septal defect; VSD = ventriculoseptal defect.

TABLE 2. *Summary of blood product usage.*

Variables	1988	1989	% change
Number of patients	177	259	+46.3
Packed red cells	802	699	−12.8
Platelet concentrate	432	293	−32.2
Cryoprecipitate	379	199	−47.5
Fresh frozen plasma	267	145	−45.7
Total units of blood products	1880	1336	−28.9

patients in Group II received less packed cells, FFP, platelets, and cryoprecipitate for every type of operation. Overall utilization of blood bank products decreased by 29%, with 1880 individual products administered in Group I patients compared with 1336 products given to Group II patients, even though there were 46% more patients in Group II.

The number of donors required to supply the blood products for each group of patients is estimated from the numbers of units of blood products administered, considering each unit of packed cells, platelets, cryoprecipitate, and FFP to have come from an individual donor. The number of donors for each patient group is presented in Figure 1 and represents the relative amount of potential exposure to the acquisition of infectious diseases for each operative group. There was an average reduction in donor exposure of 53% for Group II patients.

There were four patients in Group II with hemoglobin greater than 130 gm/L in the ICU. Two of these patients were overtransfused in the operating room and the two remaining received additional packed cells in the ICU despite a hemoglobin of greater than 110 gm/L.

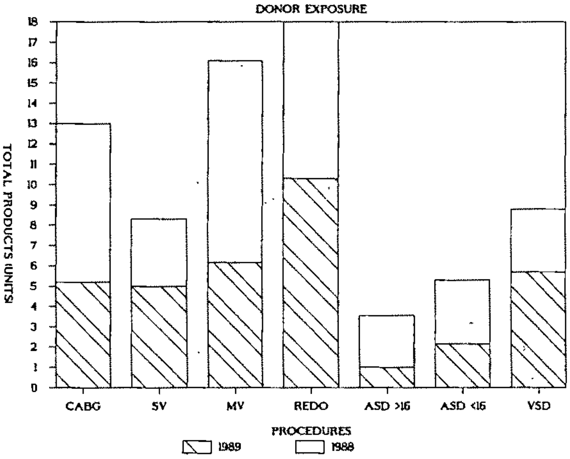

FIGURE 1. Blood usage in cardiovascular surgery. (*CABG* = coronary artery bypass grafting; *SV* = single valve replacement; *MV* = multiple valve replacement; *ASD* = atrial septal defect; *VSD* = ventriculoseptal defect.)

Discussion

The results of this study demonstrate that a significant reduction in blood bank products can be achieved by the establishment of a blood product conservation program for cardiac surgical patients. It was not possible to assess the relative contributions of the several blood conservation methods used.

We use autologous prebypass withdrawal of 1 to 2 units in patients of suitable size and hemoglobin levels. Withdrawal of autologous blood prior to bypass has been shown to result in a 20% savings in blood products, although this was accomplished in a study which aimed for a postoperative hemoglobin level of 120 to 130 gm/L and did not use other conservation methods [4]. Other objections to this method are a questionable improvement of the platelet count after retransfusion [4], and lack of applicability in small or anemic patients.

The use of blood conservation during cardiac surgery has been used with great success at the Cleveland Clinic [1]. There, patients did not receive packed red cells until the hematocrit fell below 22%. Ninety percent of their patients did not receive any blood products during hospitalization and the mean transfusion rate was 0.3 units of packed cells per patient. The major predictor of the need for transfusion was age (above 60 years) and preoperative red cell volume (below 1600 vol.%) which is related to patient weight (below

65 kg) and hematocrit (below 37.5%). We did not use a cell saver because of the effort and expense involved in saving a relatively small blood loss prior to patient heparinization. This agrees with the experience of others [5]. There are other reasons why our experience does not match the excellent results of the Cleveland Clinic. Their CABG patients required less packed cell transfusions because they were heavier with higher red cell volumes, and we did not want to withhold transfusions until a hematocrit of 22% was reached.

There is strong clinical evidence to support a program of perioperative blood product conservation, both because of the complications of transfusions as well as revised guidelines regarding the indications for transfusions. The concern about the number of donor exposures in Group I patients was a major argument in convincing staff members to reevaluate their transfusion practices. In the Western world, the fear of posttransfusion acquired immune deficiency syndrome (AIDS) has probably done more to force physicians to reevaluate and redefine safe limits in transfusion practice than have all the educational programs and research in the past decade, combined [6]. In a recent prospective study of 4163 cardiac surgical patients who received 36,282 HIV-screened components, there was one HIV seroconversion [7]. The first cases of transfusion-associated AIDS in Saudi Arabia were reported in two patients who had received blood transfusions in 1981 [8].

Postransfusion hepatitis (PTH) represents a greater viral risk from blood product transfusion. In one study [9], the incidence of PTH was 7.7% when diagnosed by elevation of serum ALT, but was only 0.07% (1% as many patients) when the diagnosis was based on clinical symptoms. Chronic hepatitis, cirrhosis, and death will occur in an even smaller percentage of patients with clinical signs of PTH. There is a high incidence of hepatitis B in Saudi Arabia, but the incidence of PTH is not known and was not examined in our study.

Other hazards from transfusion include cytomegalovirus in immunocompromised patients [10], noncardiogenic pulmonary edema in post-bypass cardiac surgical patients [11], and posttransfusion myelopathy [12].

Hemorrhage following cardiopulmonary bypass is a dangerous complication with many causes, including lack of surgical hemostasis and inadequate reversal of heparinization. The alterations in coagulation factors related to open heart surgery and cardiopulmonary bypass have been well studied. Immediately after the start of cardiopulmonary bypass there is a 50% reduction in circulating levels of platelets, fibrinogen, and factors II, VII, IX, and X due to hemodilution by the nonblood prime in the bypass machine. Factor V falls to less than 50% while factor VIII does not fall. None of these components are reduced below hemostatic levels [13].

Until recently, it was acceptable to administer blood products empirically to cardiac surgical patients to prevent or treat postoperative bleeding. The indications and limitations for the perioperative administration of blood components in surgical patients are now better defined [14–16]. The use of fewer red cell transfusions in cardiac surgery is supported by the lack of morbidity in postoperative patients who tolerate hematocrits of 25 to 30% [1,17,18]. There is considerable experience with Jehovah's witnesses who receive no blood during cardiac surgery and tolerate hemoglobin levels as low as 50 gm/L without suffering increased morbidity [19]. The safe limits for normovolemic anemia in cardiac patients have not been defined, but there is a suggestion that this may be poorly tolerated prior to anesthesia and surgery in patients with coronary artery disease [20].

No benefit has been demonstrated for prophylactic administration of FFP in cardiac surgical patients [21,22]. In fact, FFP administration may be detrimental in patients with inadequate protamine reversal of heparin and may lead to reheparinization through the re-formation of heparin–ATIII complexes [3,23].

Prophylactic platelet administration has also been shown to be of no benefit in reducing transfusion requirements in cardiac surgical patients [24]. Disorders of platelet activation and aggregation occur during cardiopulmonary bypass. In uncomplicated cases, platelet function becomes normal within one hour of the completion of bypass [13].

We recognize that our approach to improved blood conservation is a matter of educating many surgeons, residents, nurses, and anesthesiologists. This educational process will take more time before it is fully accepted by all members of the team [25,26]. In addition, all facets of the regimen of blood product conservation were not or could not be applied to all patients in Group II. Not all Group II patients underwent postoperative autotransfusion of mediastinal drainage using a cardiotomy reservoir, and it was not always possible to adhere strictly to guidelines for administration of clotting factors in patients who were actively bleeding in the ICU. Achieving normovolemic anemia has been the most difficult part of our conservation program, as shown by the fact that 70% of Group II patients had a hemoglobin level greater than 100 gm/L upon discharge from the ICU. There is certainly room for improvement in our transfusion practices for these patients, but the results reported here are still encouraging because they have led to significantly reduced exposure of these patients to unwanted complications. Future efforts will be exerted to assure more complete acceptance of our established guidelines and compliance with the principles of reducing usage of blood bank products. In addition, the use of other modalities which reduce postoperative bleeding in cardiac surgical patients, such as desmopressin and aprotinin, will be encouraged [27,28].

Acknowledgments

We thank Dr. Carlos Duran, Chairman, Department of Cardiovascular Diseases, for his guidance, and Dr. Stener Bernvil and Mr. Joseph Schifano, Blood Bank, Department of Pathology and Laboratory Medicine, for their kind assistance with this project and paper.

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Case Reports

FEMALE HEMOPHILIA A IN A SAUDI FAMILY: FAMILY STUDY AND REVIEW OF THE LITERATURE

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Hemophilia A is a sex-linked recessive disorder that is expressed in males who inherit the hemophilic gene from their mothers and a normal gene from their fathers. The incidence of hemophilia A in males varies between 1 in 5,000 to 1 in 10,000 [1,2]. Females usually transmit the disease as carriers. However, under exceedingly rare circumstances females may express the disease. We describe a Saudi girl with hemophilia A whose sister was also found to have hemophilia. To the best of our knowledge, this is the first report of female hemophilia A originating from Saudi Arabia.

Case Report

A 9-year-old Saudi girl sustained a traumatic tear of her upper gingiva just above the teeth margin posteriorly following an accidental fall. Bleeding was excessive and the child was brought to the emergency department where hemostasis was achieved by suturing the wound. The patient was discharged home but bleeding recurred the following day, and this required an additional stitch. On the third day the bleeding started again. This prompted a coagulation profile; prothrombin time was 14.9 seconds (control, 14.1 seconds) and activated partial thromboplastin time (APTT) was 53.3 seconds (normal, 26–36 seconds).

The patient's past medical history was noncontributory except for an episode of prolonged bleeding following a dental extraction a few years earlier. She had never had any previous significant trauma, surgery, or joint symptoms.

Review of the family history revealed that she has four sisters and one brother. Her father is a paternal cousin of her mother. There was a significant posttraumatic bleeding history in the maternal grandfather, and to a lesser extent in her father and brother. There was, however, no family history of hemarthrosis or spontaneous bleeding.

Because of the recurrent bleeding and the abnormal APTT, the patient was admitted to the hospital with a presumptive diagnosis of von Willebrand's disease. Physical findings were normal on admission except for a moderate amount of gingival bleeding. The initial hemogram showed WBC 6.3×10^9/L with normal differential count; hemoglobin, 122 gm/L; and platelet count, 271×10^9/L. Bleeding time was 10 minutes (normal, 4–10 minutes). She was initially managed with cryoprecipitate which resulted in prompt cessation of bleeding.

Factor VIII C level determined from pretreatment blood samples was 18% (normal, 60–200%). The posttreatment APTT was within normal limits. The patient was subsequently managed with DDAVP (desmopressin acetate) in the standard dosage and showed a good response. The remainder of the evaluation on the initial blood specimen showed normal levels of von Willebrand antigen (102%), normal ristocetin–cofactor assay (112%), and normal platelet aggregation pattern in response to ristocetin, ADP, epinephrine, arachidonic acid, and collagen. These findings indicated mild hemophilia A rather than von Willebrand disease. Because of this unexpected diagnosis, the patient underwent cytogenetic analysis which showed a normal female karyotype (46,XX). In addition, family studies were carried out on those members who could be reached.

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Accepted for publication 14 May 1990.

TABLE 1. *Results of studies on family members who could be reached.*

No.		PT[a] (control, 12.3 sec)	APTT[b] (control, 35.7 sec)	Bleeding time[c]	F VIII C	VWF[d] antigen	RICoF[e]	Platelets[f] (aggregation)
1	Father[g]	12.2	55.4	4′ 50″	14%	102%	134%	Normal
2	Mother	12.5	39.2	9′ 45″	60%	76%	134%	Normal
3	Sister[g]	11.8	54.2	12′ 10″	16%	112%	120%	Normal
4	Sister	11.8	32.8	8′ 15″	164%	112%	124%	Normal
5	Brother[g]	12.4	58.2	7′ 15″	22%	94%	120%	Normal
6	Sister	11	38.3	5′ 30″	60%	112%	100%	Normal
7	Sister[h]	--	--	--	--	--	--	--
8	Paternal grandfather	11.3	33.2	6′ 10″	217%	112%	102%	Normal
9	Maternal grandmother	12	33.1	3′ 10″	100%	94%	130%	Normal

[a] 10–15 sec; [b] 32–40 sec; [c] 4–10 sec.
[d] Factor VIII-related antigen (normal range, 60–100%).
[e] Ristocetin cofactor assay (normal range, 60–100%).
[f] Platelet aggregation in response to ristocetin, ADP, epinephrine, arachidonic acid, and collagen.
[g] Fulfills the diagnosis of hemophilia A.
[h] Could not be tested.
PT = prothrombin time; APTT = activated partial thromboplastin time; VWF = von Willebrand factor; RiCoF = ristocetin cofactor.

Results of these studies and the family pedigree are shown in Table 1 and Figure 1, respectively.

Discussion

The expression of a recessive X-linked disorder such as hemophilia A or B is rare in females, although well-documented examples have been reported. Cases have been reported in females with Turner's syndrome [3,4] and in those with a structural abnormality of the X chromosomes [5]. In females with apparently normal X chromosomes, "extreme lyonization" has been postulated as the cause of the severe clinical expression of X-linked recessive disorders [6]. In addition, the autosomal dominant transmission of hemophilia in women has been found in at least one family [7]. Homozygosity for the recessive allele is another possible mechanism for expression of a recessive X-linked disorder in a female [8]. However, the chance of a homozygous hemophilic female arising from the random or chance mating in the population at large could theoretically be disregarded, as it would be expected to occur in less than one of 100 million matings [1]. Nevertheless, such a mating may occur in a setting where consanguinity is common. Homozygosity for a hemophilia gene could also be likely in the event of a spontaneous mutation in the germline of a parent marrying into a hemophilia kindred or as the result of postzygotic somatic mutation [5].

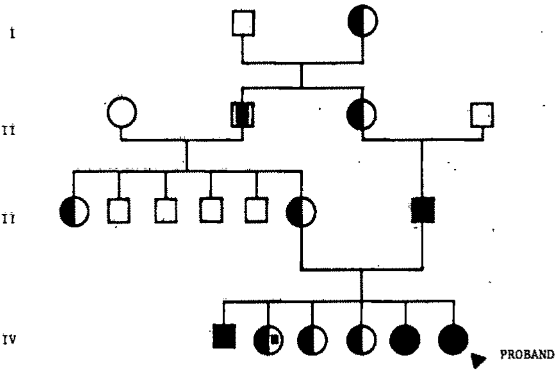

FIGURE 1. Family pedigree: □ = normal male; ■ = hemophilic male; ◨ = suspected hemophilic male; ○ = normal female; ◐ = carrier female (suspected); ○ = hemophilic female; ● = This sister could not be tested; the pattern of inheritance makes her at least an obligate carrier, but she could be a homozygous patient for the hemophilic allele (see Discussion). The numbers shown in the family pedigree represent the same numbers assigned to each family member in Table 1.

Our patient's hemophilia is likely the result of consanguinity in a hemophilia kindred. Her father is hemophilic and her mother is a definite obligate carrier, as she has a hemophilic son and hemophilic relative [9], who is both the patient's father and the mother's paternal cousin.

The patient's sister, with the low level of factor VIII, is also probably homozygous for the hemophilia gene, while the other two sisters with apparently normal levels of factor VIII are definitely obligate carriers. The patient's hemophilic sister has a slightly prolonged bleeding time, a phenomenon that can rarely occur in patients with hemophilia A [10], and this is considered secondary to her moderately severe anemia (hemoglobin, 81 gm/L) which is a known cause of such an abnormality [11]. Testing following correction of the anemia with iron supplements showed a normal bleeding time (i.e., 8 minutes once hemoglobin rose to 126 gm/L). Extreme lyonization cannot be held responsible for the low levels of factor VIII in the two affected sisters, as the family studies and the random nature of the lyonization process strongly oppose this hypothesis.

All three proven obligate carriers in this family, namely the mother and the other two sisters (Nos. 4 and 6) showed normal APTT values but wide variation in factor VIII:c levels (60 to 164%), reflecting the random nature of the lyonization process in general and the poor reliability of factor VIII:c assays alone for carrier detection.

Advanced studies using factor VIII intragenic and tightly linked DNA probes and analyzing the restriction fragment length polymorphism would help define the genetic defect responsible for the hereditary bleeding disorder in this family [2,5,12–14]. Unfortunately, this requires facilities that are not widely available.

Acknowledgment

I am very grateful to Professor A. Abdul Qader and Dr. A. K. Al-Momen for their help in performing the laboratory investigations in the patient and her family.

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RUPTURE OF SPLENIC ARTERY ANEURYSM DURING PREGNANCY: THREE CASE REPORTS WITH A REVIEW OF THE LITERATURE

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Aneurysms of the splenic artery are rare. They remain silent until rupture. Because of their frequent association with pregnancy, this is a topic of special interest to obstetricians, particularly because of the difficulty in diagnosis and because it carries a very high maternal and fetal mortality. We report three cases of ruptured splenic artery aneurysm occurring in the third trimester of pregnancy and puerperium, bringing the total number of cases reported in the literature to 75.

Case Reports

Patient 1

A 32-year-old Saudi woman (para 5, gravida 8) was admitted on 12 October 1987 at 2240 hours. Since 1300 hours she had had shortness of breath, nausea, epigastric and shoulder pain, and abdominal pain, especially over the right iliac fossa. On admission, her temperature was 37°C; pulse, 84 per minute; and blood pressure, 115/70 mm Hg. Fundal height corresponded to 38 weeks' gestation with a cephalic presentation. Fetal heart sounds were audible. The abdomen was soft, and cardiotocography showed a reactive tracing with mild uterine contractions. Vaginal examination revealed a parous cervical os, uneffaced cervix, and a high presenting part. Pulse was 80 per minute; blood pressure, 110/70 mm Hg; there was proteinuria+ but the abdomen was soft. There were no uterine contractions and no bleeding per vaginam. An intravenous line was started and the patient was given 10 mg of metoclopramide hydrochloride intramuscularly and discharged home. At 0815 hours, her condition deteriorated and she was readmitted. She was pale and hyperventilating, and her pulse had risen to 140 per minute with blood pressure dropping to 100/80 mm Hg. Her abdomen became tense and painful, and fetal parts were impossible to palpate. An urgent ultrasound was carried out which was suggestive of abruptio placentae. The patient was rushed to the obstetric theatre for emergency cesarean section. The abdomen was entered through a subumbilical midline incision and about 1,500 ml of blood was encountered in the peritoneal cavity. No bleeding source could be found.

A male infant, weighing 2,760 gm with an Apgar score of 5 at 1 minute and 5 at 5 minutes, was delivered by lower-segment cesarean section. After closure of the uterus, there was no evidence of further hemorrhage in the abdominal cavity, so the abdomen was closed. While the patient was still in the recovery room, her condition deteriorated. Her pulse rose, she became pale, and the abdomen became distended. Her hemoglobin dropped to 36 gm/L. In view of this, the abdomen was re-entered through the previous incision, which was extended upward to the left costal margin. Three liters of blood clot were found in the peritoneum. At first the bleeding was thought to originate from the liver or stomach, as the uterus was intact and well contracted, but after blood was evacuated from the abdominal cavity, it was obvious that the source of bleeding was from a ruptured splenic artery aneurysm, measuring about 3 cm and located near the hilum of the spleen. Splenectomy was carried out. The patient received a total of 18 units of blood. She and her baby, who was in good condition, were discharged home on the 28th postoperative day.

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Accepted for publication 12 May 1990.

Patient 2

A 29-year-old Saudi woman (para 5, gravida 6) had had two previous premature stillbirths and three full-term deliveries, one a cesarean section. The patient was well until 7 November 1987 at 37 weeks' gestation when she complained at 1605 hours of sudden pain in the left loin and iliac fossa that was associated with nausea. The uterus was 36 weeks in size; blood pressure was 150/80 mm Hg and pulse, 102 per minute. There was no abdominal tenderness and fetal heart sounds were heard. Hyoscine butylbromide tablets were prescribed for the patient and she was sent home. At 2330 hours on the same day, the patient was brought to the hospital in shock. She was pale, restless, and sweating. Her pulse was 140 per minute; blood pressure on arrival was 100/80 mm Hg but a few minutes later it dropped to 80/40 mm Hg. No fetal heart sounds were heard; hemoglobin was 84 gm/L; white blood count, 14.8×10^9/L; urea and electrolyte values were normal, and an electrocardiogram was normal. Ultrasound confirmed intrauterine fetal death, excluded abruptio placentae, and demonstrated intraperitoneal fluid, which was suggestive of hemoperitoneum due to a possible ruptured splenic artery aneurysm.

The patient was rushed to the operating theatre. At laparotomy, about 1.5 L of blood and clots was encountered in the abdominal cavity. The uterus was intact. The source of bleeding was the left upper abdomen, and to allow better access, a lower-segment cesarean section was carried out and a fresh stillborn 3,170-gm male infant was delivered. The bleeding was found to originate from the splenic hilum. The splenic veins were dilated and the spleen was twice the normal size. There were many adhesions with the diaphragm and these were divided. At the hilum there was a large ruptured splenic artery aneurysm (2.5 × 2.5 cm). Splenectomy with excision of the aneurysm was performed. The bleeding tail of the pancreas was also excised. The patient received a total of 11.75 L of fluid, including 6.5 L of blood, 1.75 L of fresh frozen plasma, and 3.5 L of blood substitutes. Postoperatively the patient remained pyrexial despite combined intravenous antibiotic administration. A computed tomographic (CT) scan revealed bilateral pleural effusions, lung atelectasis, a swollen edematous pancreas, and a large retroperitoneal fluid collection in the anterior left prerenal space. This suggested septic subphrenic abscess or traumatic pancreatitis. No operative intervention was undertaken. On the 24th postoperative day, the subphrenic abscess was drained by needle under ultrasound guidance; 125 ml of thick yellowish fluid was obtained. Culture was negative. However, the patient's condition deteriorated, and a laparotomy was performed on the 31st postoperative day. A small amount of seropurulent fluid in the peritoneal cavity was removed, and adhesions were divided. A kink in the proximal part of the jejunum was relieved and 7.5 cm of the jejunum, including the duodenal-jejunal flexure, was excised. The patient remained pyrexial and died suddenly 5 days after the second operation, possibly due to a pulmonary embolism.

Patient 3

A 26-year-old Saudi woman (para 2, gravida 4) was first seen at 23 weeks' gestation. She was known to have chronic active hepatitis, confirmed by liver biopsy in 1980, and gastroscopy in 1985 revealed Grade 1 esophageal varices. The patient had been maintained on prednisolone (5 mg twice daily) and azathioprine (50 mg once a day) since 1980. Liver biopsy was arranged twice in 1985, but it could not be done because of prolonged prothrombin time (PT) and partial thromboplastin time.

The blood investigations at booking indicated she was type B Rh positive, hepatitis B negative; platelets were 82×10^9/L; bilirubin, 19 μmol/L; PT, 25 (control, 16); and hemoglobin, 11.6 gm/L.

Examination revealed a palpable spleen and edema of the legs. Her antenatal course was satisfactory, except for persistent edema of the legs.

During the antenatal period the patient received, besides her previous treatment, furosemide (40 mg on alternate days) and vitamin K (10 mg daily).

At 36 weeks' gestation she was admitted to the labor ward in advanced labor, and delivered spontaneously a male infant weighing 2.8 kg. Blood loss was estimated at 100 ml. The placenta was complete and healthy. She collapsed shortly after delivery, at which time her blood pressure was 60/40 mm Hg and she had difficulty breathing. She did not lose consciousness. She complained of pain in the left shoulder. Her abdomen was soft, the uterus was firm, and there was no bleeding per vaginam. She had received no prednisolone that day and addisonian crisis was diagnosed. She was given hydrocortisone intravenously, followed by 200 ml of human albumin and Hartman's solution. Her blood pressure recovered and she seemed well, but 3 hours later she suddenly collapsed again and complained of epigastric pain. Her blood pressure was 45/25 mm Hg and respirations were labored. Hemoglobin had dropped from a prenatal level of 12.3 gm/L to 8.1 gm/L. The PT was 58 (control, 16) and platelet count was 117 × 10^9/L.

Septicemic shock or internal bleeding were considered as diagnoses, and she was transferred to the intensive care unit. Fluid was given to maintain blood pressure, but it became obvious that she was bleeding internally. Her hemoglobin fell to 40 gm/L.

In spite of the coagulopathy, a laparotomy was carried out which revealed more than 3 L of blood in the peritoneal cavity. The hilum of the spleen was discovered as the source of the bleeding, and splenectomy was performed, but generalized bleeding continued, despite all the efforts made to control it, and the patient died in the operating room.

Discussion

Splenic artery aneurysms were first described in 1770 [1], and the first reported case of splenic artery aneurysm in pregnancy was published in 1869 [2]. The first fetal survival in such a case was reported in 1928 by Mayer [3], and MacLeod and Maurice in 1940 [4] were the first who were able to save the mother. The incidence of splenic artery aneurysm noted at autopsy varies between 0.02 to 10.4% [5–12]. Stanley and Fry [10] found a 0.78% incidence of splenic artery aneurysm revealed by abdominal aortography examinations. Splenic artery aneurysms are more common in women, and splenic artery aneurysms are encountered more frequently in parous than in nonparous women [5,9,11,12].

Analysis of all cases reported in the literature [8,13–23] brought to light 75 cases of splenic artery ruptures in pregnancy. Although extremely rare, this event is more common in pregnancy. Studies have reported that 20% of ruptures occur during pregnancy [10,11,21,24,25]. Based on the incidence of aneurysms in the female population that become symptomatic during the reproductive years, it has been calculated that between 6.6 to 10% will rupture during pregnancy [9,12,13,20,21,22,24]. Of the 75 cases reported, 69.3% ruptured in the third trimester, 8% in the second trimester, 8% during labor, and 14.7% postpartum. The maternal mortality rate is 64% and fetal mortality rate, 72.2%. The survival rate of the mother and infant combined is 18.7% (14 cases, including one of the three reported here).

The pathogenesis of these aneurysms is not clear. The lesions are generally regarded as congenital, with the atherosclerotic changes superimposed on the congenital defect [9,10,26-30]. Pregnancy seems to precipitate enlargement of the aneurysm, which makes it more liable to rupture. The hormones secreted during pregnancy may also weaken the vessel wall, and this is compounded by the increased blood volume and cardiac output of pregnancy leading to increased intraluminal pressures [31]. The rupture may occur in two stages. There may be an initial small leak which stops, and then hours or even weeks later a further hemorrhage which may be massive. This sequence has been observed in 25% of the cases [9,10,16,17,32].

Spontaneous rupture of a splenic artery aneurysm in the third trimester of pregnancy is a catastrophic event. There is sudden severe pain in the epigastrium and left hypochondrium. The pain is occasionally referred to the shoulders and back, and may be accompanied by nausea and vomiting. At onset, tenderness and muscular rigidity are limited to the epigastrium and left hypochondrium. As hemorrhage progresses, blood escapes into the general peritoneal cavity from the lesser sac and an acute surgical abdominal crisis develops. In the cases reviewed, the outstanding symptom at this time is severe abdominal pain (32 cases). The pain was epigastric in 27 cases, it was located in the shoulders in 13, and it radiated to the back in three. Vomiting was a common symptom (17 cases). All patients eventually showed signs and symptoms of shock, but no external evidence of bleeding.

A few patients have intermittent pain for a few days or weeks before rupture. History of pain or syncope followed by recovery is a significant indication. The initial rupture occurs into the lesser sac, with accompanying pain or syncope, and a hematoma temporarily tamponades the bleeding aneurysm, lasting for minutes to some weeks. The hematoma eventually ruptures with an exsanguinating intraperitoneal hemorrhage through the foramen of Winslow [16,32-34]. If double rupture occurs, the partial tamponade allows time for diagnosis and preparation for intervention. Patient 1 probably had a two-stage rupture. The first episode was apparently confined to the lesser sac, with typical symptoms of sudden severe epigastric and shoulder pain, nausea, and dyspnea lasting for approximately 10 hours. This was followed by 7 hours of recovery until the second rupture, which exhibited the clinical picture of intraabdominal hemorrhage. Patient 2's condition was also suggestive of double rupture, the first accompanied by sudden severe epigastric pain and nausea, followed by recovery lasting for about 7 hours, and then a second hemorrhage that entered the greater peritoneal cavity and precipitated shock. Our third patient also demonstrated double rupture. Her first rupture occurred shortly after delivery, followed by recovery and then 3 hours later collapse.

Berger et al [35] and Greene et al [36] recommend aortography as a reliable diagnostic method in patients with a latent period between episodes of bleeding who are suspected of harboring an aneurysm of the splenic artery, such as the case described by Gillam [37].

The difficulty in making a correct diagnosis prior to laparotomy is understandable because of the many obstetrical complications that simulate rupture of a splenic aneurysm, most of them more frequently encountered conditions. In early pregnancy, it resembles a ruptured ectopic pregnancy and in advanced pregnancy mimics ruptured uterus, abruptio placentae, intraabdominal trauma, complication of ovarian cyst, bleeding from ectopic decidua, gastrointestinal hemorrhage, and bleeding from a hepatoma. The preoperative diagnosis was premature separation of the placenta in 11 cases and uterine rupture in seven cases. Most were diagnosed as intraabdominal hemorrhage of unknown origin. A lesion of the spleen was suspected in 12 cases but a ruptured splenic aneurysm was diagnosed preoperatively in only three [22,27,31]. Nine of the 12 mothers survived and this emphasizes the importance of the primary recognition of such a rare occurrence. In six cases, fetal distress led to immediate cesarean section, at which bleeding in the peritoneal cavity was discovered and diagnosis made.

In our Patient 1 a diagnosis of abruptio placentae was made and in Patient 2, intraabdominal hemorrhage due to ruptured splenic artery aneurysm. However, in the first case both mother and baby survived and in the second both mother and baby died, the mother dying some weeks later from postoperative complications. Patient 3's medical history confused the clinical picture and led to delayed surgical intervention, with massive internal bleeding the outcome.

If at laparotomy the more obvious diagnosis is not confirmed, the incision should be extended to allow a thorough exploration with particular attention directed toward possible sites of aneurysm formation. In such emergency cases a midline incision is far superior to a Pfannenstiel. Survival depends on prompt recognition of the condition and treating by ligation of the splenic artery proximal to the aneurysm, removing the spleen, and restoring blood volume. All reported maternal survivors who underwent operation for ruptured splenic artery aneurysm when pregnant had splenectomies.

Acknowledgments

I am grateful to Miss Julie Zdanowicz and Miss Julie Moore for their help in typing this paper. I am also indebted to Dr. W. G. Paterson, Senior Consultant, for his valuable advice and criticism and to all colleagues in the Department of Obstetrics and Gynaecology for access to the records of patients under their care.

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AN UNUSUAL CASE OF ABDOMINAL PAIN: PANCREATIC TUBERCULOSIS

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Tuberculosis is commonly seen in the populations of developing countries. Despite recent advances in diagnostic techniques, patients with extrapulmonary tuberculosis continue to pose a diagnostic dilemma [1–3]. Pancreatic tuberculosis is rare and may mimic a malignant lesion or chronic pancreatitis originating from other infective causes [4]. We describe a patient with chronic abdominal pain caused by tuberculosis of the pancreas.

Case Report

A 30-year-old unmarried Indonesian woman had experienced vague abdominal pain for one month. The pain was mainly located in the upper abdomen and had gradually intensified. No temporal relationship to meals was noted. She denied any history of vomiting, hematemesis, jaundice, melena, fever, night sweats, or change in bowel habits. She had lost 3.0 kg and her appetite was poor. She did not smoke or consume alcohol.

Examination revealed an unwell woman who showed no evidence of anemia or jaundice. There was also no peripheral edema, clubbing, or cyanosis. Cardiovascular and respiratory findings were all normal. Abdominal examination revealed mild tenderness in the epigastrium. There was no organomegaly or ascites. Rectal findings were unremarkable.

Laboratory investigations showed the following values: hemoglobin, 11.8 gm/L, and white blood cell count, 9.3 × 10^9/L, with normal differential and platelet count of 338 × 10^9/L. Serum electrolyte values as well as liver function tests were normal. Serum amylase level was 2.23 μkat/L (reference interval, < 3.66 μkat/L.) X-ray films of the chest were normal but an ultrasound scan of the abdomen showed a hypoechogenic mass measuring approximately 5 × 5 cm involving the head of the pancreas extending up to the hilum of the right kidney (Figure 1). No stones in the gallbladder or common bile duct were visible. A contrast-enhanced computed tomogram of the abdomen showed a hypodense mass involving the head of the pancreas. There was no secondary involvement noted in the liver (Figure 2).

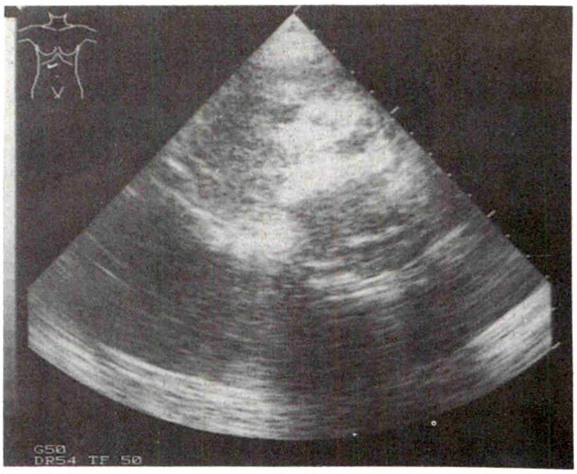

FIGURE 1. Ultrasound scan of the upper abdomen.

Ultrasound-guided fine-needle aspiration biopsy was used to obtain a specimen of the pancreatic mass. Cytological evaluation of the specimen revealed normal ductal epithelial cells with occasional polymorphs and plasma cells. There was no evidence of malignancy.

An exploratory laparotomy was performed and a large mass measuring 5 × 5 cm was found that was firm to hard. The mass involved the head of the pancreas. There were several enlarged lymph glands in the mesentery and omentum. Frozen

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Accepted for publication 20 June 1990.

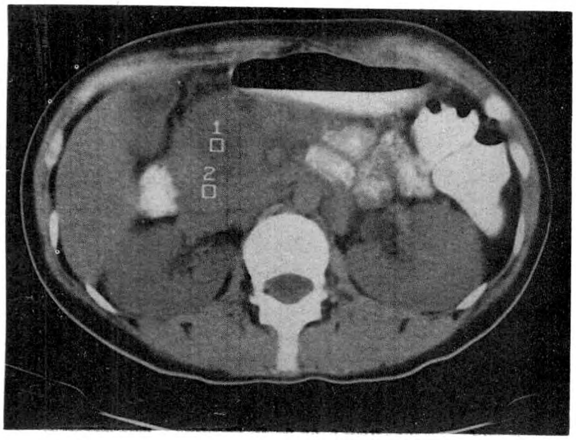

FIGURE 2. Computed tomographic scan of the abdomen.

section biopsy specimens were obtained from the glands and the mass in the pancreatic head that showed some granulomatous lesions with epithelial cells and central caseation. Auramine-rhodamine-stained specimens examined by fluorescent microscopy were positive for tubercle bacilli. Postoperatively the patient made an uneventful recovery. She was begun on rifampicin, ethambutol, and isoniazid with pyridoxine. She was discharged home on the twelfth postoperative day. During the subsequent one year of follow-up she remained asymptomatic and gained 5 kg. At the end of one year, ultrasound scan showed normal pancreatic size and configuration.

Discussion

In the developing world, tuberculosis is a common health hazard [5,6]. Alimentary tract tuberculosis is elusive and difficult to diagnose [4]. In miliary tuberculosis, the liver, spleen, intestine, and abdominal lymph nodes are commonly affected, but involvement of the pancreas is uncommon. Paraf et al [2] in an autopsy series found a 2.1% incidence of pancreatic or peripancreatic involvement in areas of the world where there is a high incidence of tuberculosis. In a series of patients from India, Bhausali [1] did not find any cases of pancreatic tuberculosis among 300 cases of tuberculosis.

Abdominal tuberculosis may occur without any focal lesion in the lung [7], as in our patient. As tuberculosis was not considered in the initial evaluation, no tuberculin test was done. However, the tuberculin test may be negative in as many as 50% of the cases of abdominal tuberculosis and even in miliary tuberculosis [7].

Pancreatic involvement by tuberculosis may result from several mechanisms. Hematogenic spread from the primary focus is responsible for most cases. Direct involvement of the pancreas by mycobacteria tuberculosis is rare [8]. New imaging techniques such as ultrasound and computed tomography may indicate a mass in the organ but not confirm its nature. Even fine-needle aspiration biopsy can fail to establish a tissue diagnosis [8], as witnessed in our patient.

Tissue diagnosis was only achieved after an exploratory laparotomy. Even in developed countries where tuberculosis is uncommon, pancreatic tuberculosis should be considered in a patient who has chronic abdominal pain and a pancreatic mass. The mass in our patient was thought initially to be a pancreatic tumor. Our case is unique as tuberculosis of the pancreas is a rare but treatable condition.

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TRACHEOESOPHAGEAL FISTULA, ESOPHAGEAL ATRESIA, AND LEFT PULMONARY AGENESIS

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The incidence of pulmonary agenesis is one in 10,000 to 15,000 autopsies [1,2], and the incidence of tracheoesophageal fistula with esophageal atresia is one in 4500 births [3]. The occurrence of both in the same patient is correspondingly rare. We report the management of such a case and suggest a change in the surgical approach to minimize the complications encountered.

Case Report

A 2000-gram female infant was referred at 24 hours' age because of frothing, cyanosis, and respiratory distress. When seen on admission the baby was cyanosed and tachypneic. Auscultation of the chest showed no air entry on the left side and wheezing and crepitations on the right. The apex beat was felt in the left axilla. Abdominal findings were normal. A 10F red rubber catheter was arrested 10 cm from the gum margin.

Chest x-ray study showed an opaque left hemithorax with shift of the heart to the left, an emphysematous right lung with patchy consolidation, and only ten pairs of ribs with anomalies in the upper five thoracic vertebrae (Figure 1). The baby was ventilated mechanically and a gastrostomy done under local anesthesia. Serial chest x-ray studies showed there was no aeration of the left lung. Bronchoscopy done on day 4 showed a blind-ending left bronchus that was 1 cm long. Computed tomographic (CT) scan of the thorax confirmed the complete absence of pulmonary tissue on the left (Figure 2). On day 11 the baby underwent right thoracotomy, ligation of the tracheoesophageal fistula, and esophageal anastomosis. Postoperatively the baby was ventilated. The baby had three episodes of airway obstruction during ventilation, necessitating bronchoscopic clearance of necrotic debris and crusts which collected mainly in the blind-ending left bronchus. Postoperative chest roentgenograms showed patchy pneumonitis of the right lung. A Gastrografin swallow nine days after surgery showed an intact anastomosis. In addition there was a gradual rise in blood urea and serum creatinine levels from admission levels despite an initially normal urine output. The baby became anuric 10 days following thoracotomy and died of septicemia four days later. No investigations were done to determine the cause of renal dysfunction.

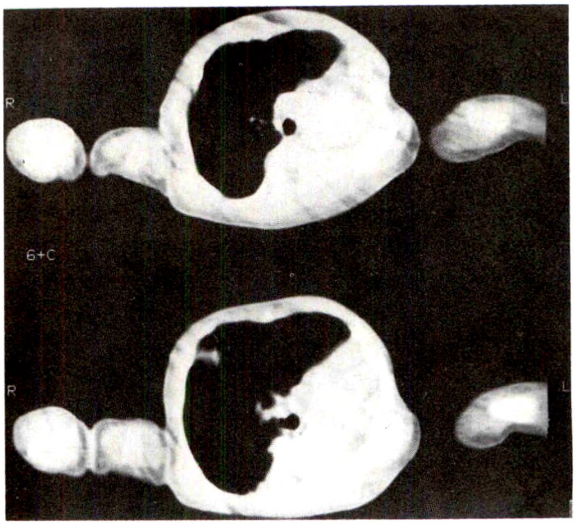

FIGURE 1. Chest x-ray study (anteroposterior view), showing opaque left hemithorax, emphysema in the right lung, pneumonitis, and upper thoracic vertebral anomalies with only 10 pairs of ribs.

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Accepted for publication 20 June 1990.

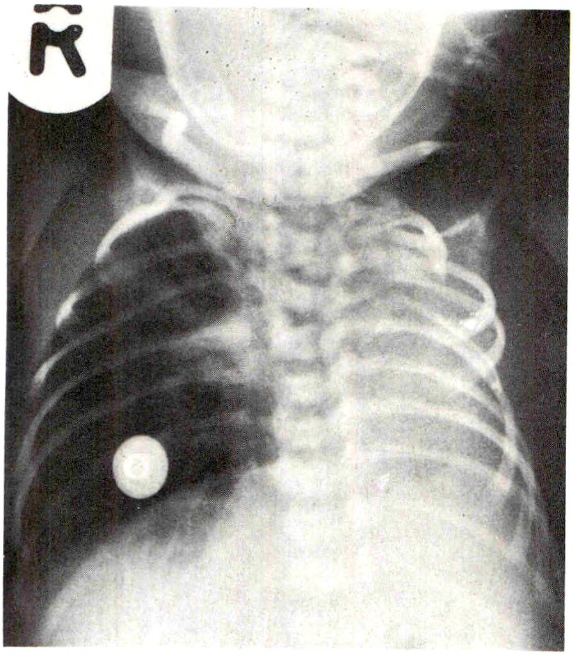

FIGURE 2. Computed tomographic scan of the chest at the level of the carina showing heart in the left hemithorax, no left lung, and emphysematous right lung.

Discussion

Esophageal atresia with or without tracheoesophageal fistula and pulmonary agenesis is an uncommon association; only 17 cases have been reported. Of these, 14 cases had esophageal atresia, tracheoesophageal fistula, and unilateral pulmonary agenesis [4–7]. The right lung was absent in nine patients and left lung in five. Pulmonary agenesis and esophageal atresia are both commonly associated with the VACTERL group of anomalies [8]. Spencer [9] modified the morphological classification of pulmonary agenesis. Our patient had a carina and rudimentary left bronchus and was classified into group 2b. The diagnosis of unilateral pulmonary agenesis can be confirmed by bronchoscopy, bronchography, radionuclide scan, and angiography. In our case the diagnosis was established by bronchoscopy and confirmed by CT scan. Of the 14 cases so far described, there has been only one survivor who had tracheoesophageal fistula and right pulmonary agenesis and who was treated successfully by delayed primary anastomosis [7]. The existence of left pulmonary agenesis with a rudimentary left bronchus poses certain special problems: (1) thoracotomy on the same side as the solitary functioning right lung fosters the risk of respiratory complications and contributes to a poorer prognosis, and pooling and encrustation of secretions in the blind left bronchus contributed to recurrent episodes of respiratory obstruction on ventilation and infection in the right lung. Preserving the function of the solitary lung and avoiding respiratory complications are crucial in a baby with unilateral pulmonary agenesis. Hence, retrospectively we suggest that a thoracotomy should be performed on the same side as the pulmonary agenesis whether located on the right or left. It is possible to ligate the fistula and perform a satisfactory anastomosis from the same side as the aortic arch, though this is technically more difficult. This will avoid fatal lung complications in the solitary functioning lung. It may also be possible to excise the blind bronchus to prevent pooling of secretions and respiratory infection. Delayed primary anastomosis remains the best treatment in babies with tracheoesophageal fistula, esophageal atresia, and pulmonary agenesis.

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ASSOCIATION OF PRIMARY BILIARY CIRRHOSIS AND PROGRESSIVE SYSTEMIC SCLEROSIS IN A SAUDI PATIENT

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Primary biliary cirrhosis (PBC) is a chronic, slowly progressive liver disease of unknown etiology that mainly affects middle-aged women. Its main features include pruritus, jaundice, melanosis, steatorrhea, and hyperlipidemia. Progressive systemic sclerosis (PSS) is a chronic connective tissue disease also seen in middle-aged women and characterized by symmetrical skin induration and multisystem involvement. The association of PBC with CREST (variant of scleroderma) has been described before [1]. CREST is characterized by *c*alcinosis, *R*aynaud's phenomenon, abnormal *e*sophageal motility, *s*clerodactyly, and *t*elangiectasia. We report a case of PBC with progressive systemic sclerosis but without the CREST syndrome.

Case Report

A 47-year-old woman was initially seen because of tightness of her skin over her arms and legs as well as the trunk. Progressive systemic sclerosis had been diagnosed 15 years before. She described a history of Raynaud's phenomenon, muscle cramps, and inability to open her mouth properly. Over the last 6 months she had noted progressive generalized itching over her entire body with darkening of her urine. There was no history of hepatitis, alcohol ingestion, or blood transfusion.

She was on prednisone (10 mg daily) and ibuprofen as well as nifedipine for her high blood pressure. Clinical examination revealed tight, indurated skin over her extremities and trunk, with loss of hair on her appendages. She was mildly jaundiced and had bilateral swollen parotid glands. There were no spider nevi or xanthelasma. She could only open her mouth to 3.5 cm. She had telangiectasia over her tongue and lips. Lung findings were normal and cardiovascular examination revealed a Grade II/IV systolic murmur over the pulmonary area with accentuation of the pulmonary component of the second heart sound. The liver was two fingers below the costal margin and liver span was 16 cm. Ascites was present.

The following laboratory findings were normal: full blood count, thyroid function test, prothrombin time and activated partial thromboplastin time, antinuclear antibodies, rheumatoid factor, serum complement, creatinine phosphokinase, and aldolase. Brucella titer, hepatitis B markers, and schistosoma titer were negative. The anti-smooth muscle antibodies and antimitochondrial antibodies were positive. Liver function test showed bilirubin, 60 μmol/L. Alkaline phosphatase was 876 IU/L; alanine transaminase (ALT), 373 IU/L; and aspartate transaminase (AST), 267 IU/L. Albumin content was normal.

Urine was positive (+++) for urobilinogen. Barium swallow and follow-through was normal. Pulmonary function test showed marked reduction in diffusing capacity and restrictive airway disease. Skin biopsy showed dermal fibrosis consistent with scleroderma. The diagnosis of systemic sclerosis with a probability of primary biliary cirrhosis, as evidenced by her clinical picture, liver enzyme values, and serological findings, was suggested. A needle biopsy specimen of her liver showed features of chronic liver disease compatible with primary biliary cirrhosis (Figure

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Accepted for publication 12 June 1990.

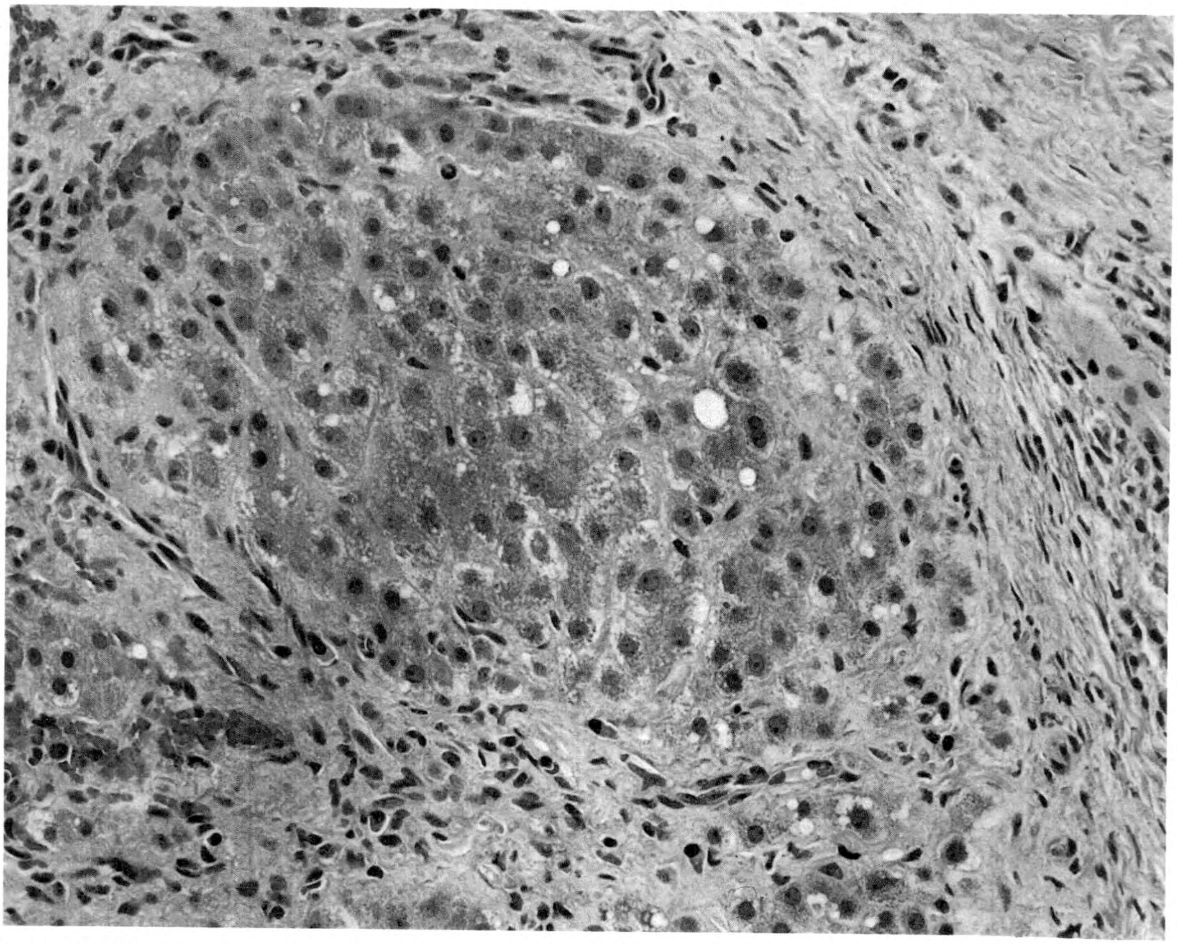

FIGURE 1. Liver biopsy showing portal fibrosis, loss of interlobular ducts, and mild portal inflammation. The parenchymatous nodule revealed mild steatosis. (H&E; original magnification, × 250.)

1), and sections of the specimen revealed irregular portal and periportal fibrosis. There were also rare interacinar ducts and they were poorly preserved, with some exhibiting lymphocytic infiltration. Cholangiolar proliferation was moderate. The lymphocytic infiltrates were scanty and the piecemeal necrosis was mild. The periportal hepatocytes contained copper particles, as revealed in rhodamine-stained sections (Figure 2). There was mild steatosis. These collective histological findings were considered consistent with the diagnosis of PBC. The patient was put on colchicine (0.6 mg orally twice daily) and evaluated at three and six months, at which time she showed good clinical response. Enalpril was started after liver biopsy to control hypertension. Her jaundice and itching disappeared and her urine color returned to normal. Her liver function test showed bilirubin, 20 IU/L; alkaline phosphatase, 116 IU/L; ALT, 249 IU/L; and AST, 178 IU/L.

Discussion

The prevalence of PBC in Great Britain is 40 to 54 cases per million population, whereas in Sweden it approaches 92 million [2]. In Saudi Arabia the exact incidence of PBC is not known, but in our own experience at this tertiary care center, both PBC and scleroderma appear to be uncommon.

The degree of association depends on whether PBC or PSS is the index disease. In studies where PSS was the index disease, negligible numbers of cases of chronic liver disease were found [3,4]. Bartholomew et al [4] found only eight cases of chronic liver disease among 727 cases of

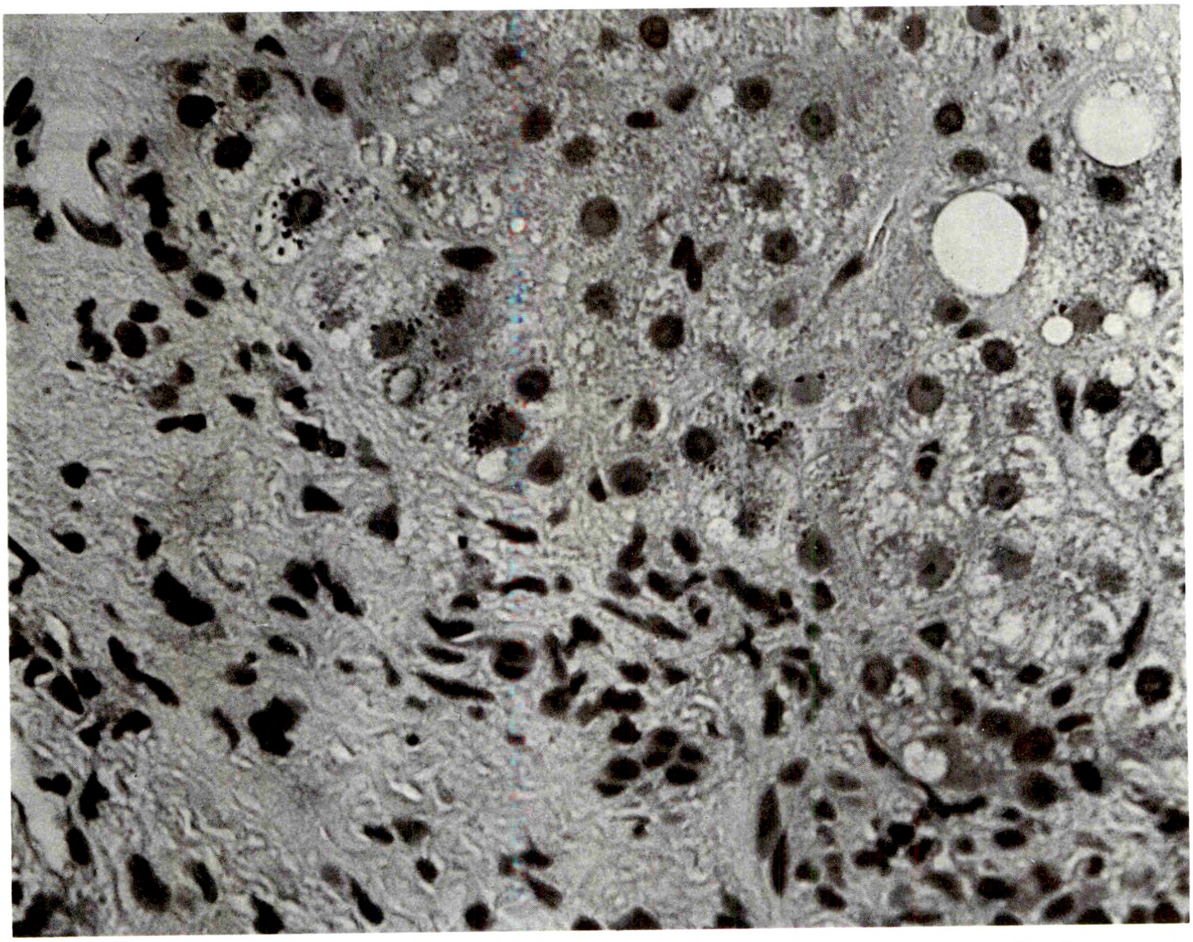

FIGURE 2. Liver biopsy showing copper particles in periportal hepatocytes and portal fibrosis. (Rhodamine stain; original magnification, × 450.)

scleroderma, while D'Angelo et al [3] found a comparable number of cases of cirrhosis in scleroderma patients and controls. This contrasts with series in which PBC was the index disease, with a prevalence of 3 to 17% [5,6]. In these series, scleroderma was generally mild. However, a few, as in our patient, had evidence of abnormal pulmonary function. Our case had clinical findings of pulmonary hypertension and a marked reduction in diffusing capacity.

In the liver biopsy of this patient, classic granulomas or duct lesions pathognomonic of PBC were not demonstrated, but ductopenia, portal fibrosis, along with inflammation and only mild piecemeal necrosis plus increased copper concentration in the periportal hepatocytes and scanty lymphocytic infiltration in the ductal epithelium, all are consistent with the diagnosis of PBC.

The patient described here has manifested clinical and laboratory features of PBC 15 years after PSS was diagnosed. In 1971 Reynolds et al [1] reported on the relationship between PBC and CREST syndrome, and O'Brien et al [7] reported a case of scleroderma without CREST. Since then, many case reports have appeared in the literature [8,9].

Treatment of PSS has been unsatisfactory; however, both colchicine [10] and D-penicillamine treatment in PBC have produced conflicting results. A recent report failed to show any therapeutic benefit from these drugs [13]. Other investigators have recommended colchicine in the treatment of PBC [14] and also reported that its use led to improved survival in patients with cirrhosis of the liver [15].

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Letters to the Editor

The *Annals of Saudi Medicine* welcomes letters to the Editor from its readers. They may be on any topic, though the Editor especially encourages discussion of papers published in the *Annals*. Letters should be no more than 100 typewritten lines in length, typed double-spaced, and submitted in triplicate. Letters may include one figure or brief table and up to five references. Submission of a letter constitutes permission for the *Annals* to use it for publication, and letters should not duplicate similar material being submitted or published elsewhere, and the *Annals* reserves the right to edit letters submitted. Letters referring to a recent *Annals* article should be received within 6 weeks of the article's publication.

The Usual and Unusual Presentation of Ewing's Sarcoma

To the Editor: It was with great interest that I read the article by Dr. Shaheen et al [1]. Noting that this article originates from a division of orthopedics and to a large extent consists of a description and discussion of the radiological appearance of Ewing's sarcoma, I was concerned that there was no evidence that the authors had involved one of their radiological colleagues in the study.

Textbook classifications of Ewing's tumors are commonly based on the "radiological" appearances. In the article, a subgroup of cortical Ewing's tumors is mentioned, with these two cases showing "partial subperiosteal necrosis." However, subperiosteal necrosis cannot be diagnosed on an x-ray study; and certainly, partial subperiosteal necrosis can only be judged by a pathologist. Unfortunately, there is also no evidence that a pathologist was involved in reviewing the material of the study. In the book by Aegerter and Kirkpatrick [2], referenced by Shaheen et al, the following comment is made: "Ewing's tumor is a malignant neoplasm that always arises in medullary tissue." This statement is supported by Shaheen et al's Figure 3B which, unlike the description by Aegerter and Kirkpatrick, shows a density of the medullary cavity higher than that of subcutaneous fat and similar to that of muscle which is consistent with tumor involvement of medullary tissue.

According to the newest concepts, the origin of Ewing's sarcoma is still uncertain, possibly neuroectoderma [3]. The tumor consists of undistinguished small round cells and may be found outside the bone (extraosseous Ewing's sarcoma) [3]. When originating from the bone, the medullary cavity usually is the primary affected site, the epiphysis being an unusual site [3]. Pathologically the differential diagnosis includes malignant lymphoma, metastatic neuroblastoma, and other undifferentiated cancers [3]. Radiologically, the differential diagnosis between malignant lymphoma and Ewing's sarcoma is also difficult and this could have been mentioned in the Discussion.

In Figure 4A, a patient with painful swelling of the right scapular region is presented. The legend for the computed tomographic scan in Figure 4B describes almost complete destruction of the scapula, but the appearance of the CT image suggests the contrary—that the right scapula is intact and the left scapula is affected by destruction.

These criticisms would have been avoided if the authors had included colleagues from radiology and pathology in their study.

Acknowledgments

I wish to thank Dr. T. Mygind, Consultant Radiologist, King Faisal Specialist Hospital and Research Centre, for reviewing the contents of the letter.

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Fluid Therapy in Diabetic Ketoacidosis: Comparative Study

To the Editor: A life-threatening emergency, diabetic ketoacidosis, is a unique state of hyperglycemic hypertonic dehydration accompanied by ketotic acidemia. Its incidence is not declining and represents 67.2% of our population of newly diagnosed diabetic children in Riyadh. Treatment remains difficult, and mortality reported in the literature is still high, particularly in young children below 5 years of age and those with new onset [1,2,5]. The sudden development of cerebral edema, confirmed by computed tomography or on postmortem examination, during the first 24 hours of reasonable therapy for severe diabetic ketoacidosis remains poorly differentiated [1–5]. Contradictory reports have appeared that attempt to relate its occurrence to specific aspects of treatment, particularly to the overall fluid administration during the first 24 hours [3–5].

We compared retrospectively two groups of patients treated with two different rehydration therapy protocols and administered by the same diabetic team at Suleimania Children's Hospital. Diagnosis of diabetic ketoacidosis was based on clinical findings (vomiting, abdominal pain, acidotic breathing, moderate to severe dehydration, torpor, or coma) and biological features (hyperglycemia > 15 mmol/L or 270 mg/dl) ketonuria, and metabolic acidosis (bicarbonate level, < 15 mmol/L). We reviewed the medical records of 38 patients of both sexes admitted to Suleimania Children's Hospital between 1987 and 1989 with a comparable mean age of onset (6 years 5 months in Group 1, 5 years 8 months in Group 2). The patients were newly diagnosed diabetics and presented similarly at onset with moderate to severe diabetic ketoacidosis. In 52.6% (20/38), metabolic acidosis was severe with pH < 7.1. Laboratory investigations and monitoring in the first 24 hours were similar for both groups. Blood gas analysis (capillary) and Hemoglukotest (using Reflolux 11 M device) were done every half hour for the first three hours, then hourly for the next 3 hours, then every three hours. Serum urea and electrolyte concentrations were determined initially and after three hours, then every four to six hours. Random urine electrolyte analysis was done initially and after 3 hours. Urine was examined for glucose, and ketone was tested whenever urine was passed. Urine output was monitored in the initial 24 hours of treatment in all patients. The protocol used in the 15 patients who made up Group 1 consisted of rehydration using an initial volume of 20 to 40 ml/kg over the first 2 hours then 3 L/m^2 over the remaining 22 hours using initially normal saline then ¼ normal saline D 5 % when blood glucose level reaches 16.6 mmol/L (300 mg/dl). For protocol 2, which comprised 23 patients, 5 to 10 ml/kg of normal saline was infused rapidly only if signs of shock were present, until correction of oliguria, turgor time, and blood pressure. Over 24 hours, the volume of fluids infused was 1 .5 L/m^2 (in cases of moderate dehydration) to 2 L/m^2 (in cases of severe dehydration). Intravenous fluids were given and initially consisted of normal saline when the corrected serum sodium level was below or equal to 140 mmol/L, ½ normal saline when the corrected serum sodium level was about 150 mmol/L, and ¼ normal D 5% when the blood glucose level reached 16.6 mmol/L (300 mg/dl). Corrected sodium was calculated by adding 2.75 mmol/L of sodium for each 5.55 mmol/L (100 mg/dl) of glucose above 5.55 mmol/L, i.e., 1 mmol sodium for 2 mmol of glucose [3,4]. Insulin therapy using continuous intravenous infusion of soluble insulin through a pump at a dose of 0.1 U/kg stat then 0.1 U/kg/hour then 0.05 U/kg/hour when blood glucose level reached 16.6 mmol/L (300 mg/dl) was similar for the two groups of patients. Likewise, in both protocols, the initial intravenous fluid contained 20 mEq/L of potassium chloride in the absence of anuria or cardiovascular instability related to hyperkalemia, then 40 mEq/L when urine was passed. Finally, small doses (20 to 40 mEq/m^2/over 2 hours) of bicarbonate were infused intravenously, done similarly in both groups, when pH was below 7.1.

For both groups of patients, clinical improvement was observed in the subsequent 6 to 12 hours of therapy, without complications. The blood glucose level declined, and the time of normalization of metabolic acidosis and variations in the serum potassium level were also similar in both groups. The intravenous fluids given in the two protocols differed significantly: 61 ± 11 ml/kg/day, i.e., 1265

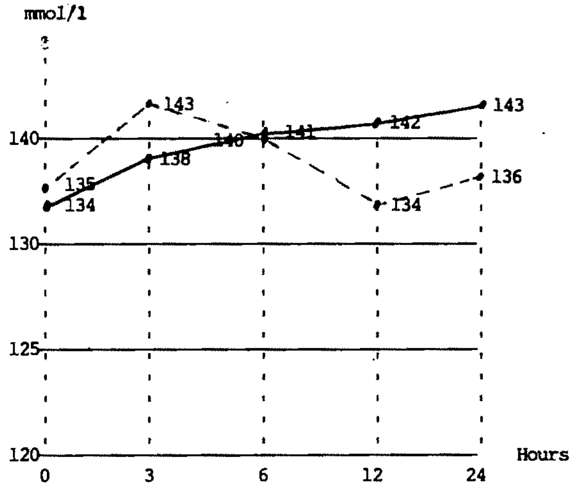

FIGURE 1. Variations in corrected serum sodium levels during the treatment of diabetic ketoacidosis. (Protocol 1 = broken line; Protocol 2 = solid line).

to 1822 ml/m^2/day (protocol 2) versus 124 ml ± 13 ml/kg/day, i.e., 3164 to 3433 ml/m^2/day (protocol 1) ($P = 0.001$). The serum sodium level at onset ranged from 120 to 141 mmol/L. The variations in the corrected serum sodium levels were different (Figure 1). In protocol 2, there was neither a sudden drop nor hypernatremia and the serum sodium level increased steadily throughout the treatment. In protocol 1, there was no steady rise (Figure 1). Polyuria of short duration was noted in only two patients in the two groups during the first hours of treatment. Urine output was normal in all patients, even for those who were severely dehydrated during the first 24 hours of treatment.

Factors implicated in the development of brain edema include osmotic dysequilibrium between intracellular and extracellular brain water; impairment of blood-brain integrity with shrinkage of the endothelial cells of the cerebral capillaries and opening of the tight junction [1–5]; osmoprotective brain adaptation with creation of idiogenic osmoles in the cytosol resulting in a net gain of cell water [3,4]; and excessive secretion of antidiuretic hormone which retains free water, aggravates dilutional hyponatremia, and shifts intracellularly the excess of fluids (particularly when hypotonic) administered [3,4]. Aggravating factors were rapid blood glucose decline (more than 5.55 mmol/L/hour, i.e., 100 mg/dl/hour), an aggressive bicarbonate therapy leading to paradoxical central nervous system acidosis, and cerebral vasconstriction [1,3,4]. On the other hand, during therapy for diabetic ketoacidosis with steady fluid and insulin administration, osmotic urine loss is brief and a "hidden" oxidation source of endogenous water exists in the form of water generated by glucose oxidation and ketone metabolism [4]. However, these different factors did not agree with the clinical observations of cerebral edema in a recent study [5]. However, it is actually universally accepted that correction of the metabolic acidosis and hyperglycemia should be gradual during treatment of diabetic ketoacidosis [1,2]. Similarly, in our opinion, the correction of dehydration should be slow, despite the contradictory reports about the precise mechanisms of cerebral edema. Duck and Wyatt [3] proposed as a guideline a maximum of 4 L/m^2/day compared with the previously recommended 6 to 8 L/m^2/day [3]. However, Harris et al [4] considered that even 4 L/m^2/day would provide an excessive volume too quickly in some patients [4]. Our study shows that a fluid volume (although markedly smaller) of 1.5 to 2 L/m^2 should be enough to correct moderate to severe dehydration in diabetic ketoacidosis, with special attention given to the trends of corrected serum sodium during treatment. Indeed, failure to normalize real and corrected serum sodium levels or its sudden drop are a potential danger sign and indicate dysregulation of endogenous vasopressin [3,4]. In our series, monitoring of the corrected serum sodium level showed a steady increase in Group 2 compared with Group 1 patients. Furthermore, clinical and metabolic improvement were similar in the two groups of patients, without complications, despite the significant fluid reduction carried out in Group 2.

Until the precise mechanisms of cerebral edema in diabetic ketoacidosis are known and effective prevention is instituted, fluid therapy, though individualized and adapted to each patient, should be slow and steady, given under close monitoring of the corrected serum sodium values, and associated with a gradual correction of hyperglycemia and metabolic acidosis.

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Pulmonary Function Tests in Saudi Patients With Rheumatoid Arthritis

To the Editor: It is well known that the pleura and lung are frequently involved in rheumatoid arthritis and that a variety of functional abnormalities of the lung have also been reported [1,2].

We determined dynamic lung volumes (FVC, FEV1) and arterial blood gases in 23 consecutive Saudi patients with rheumatoid arthritis seen at Asir Central Hospital. There were 22 females and 1 male. Age range was 20 to 75 years (mean, 46 years). All patients had rheumatoid arthritis according to criteria published by the American Rheumatism Association [3], but exhibited no respiratory symptoms and had normal chest radiographs. Joint symptoms had been present for between 5 months and 20 years (mean, 6.8 years). Table 1 summarizes the patient data.

Using a Vitalograph, the best of three values was recorded for FVC and FEV1. Unfortunately the test could be done properly in only 15 patients. Arterial blood gases were determined in all patients.

Eight patients had hypoxemia ($PaO_2 < 60$ mm Hg, for Abha with an altitude of 2800 meters). Hypocapnia ($PaO_2 < 35$ mm Hg) was noted in 15 and respiratory alkalosis in three.

Spirometric values were within normal limits for Saudis in 12 of 15 patients [4]. None of our patients were smokers and no obstructive airway disease was detected, contrary to the findings of Geddes et al [5] who found that obstructive airway disease was the most common form of pulmonary involvement in rheumatoid arthritis. They speculated that these abnormalities could be secondary to previous bronchiolitis. Like us, Oxholm et al [6] were not able to reproduce their results. However, these later investigators found that spirometric values and arterial blood gas findings were normal in asymptomatic rheumatoids with normal chest x-ray studies, a finding different from ours. The only abnormality they detected was a reduction in the transfer factor, a test which we could not perform.

TABLE 1. *Age and sex distribution of rheumatoid arthritis patients.*

Patient No.	Sex	Age (yr)	Duration of joint symptoms (yr)	Rheumatoid factor	Joints involved
1	F	20	7	Positive	Small & large, spine
2	F	38	8	Positive	Small & large
3	F	60	10	Positive	Small & large
4	F	20	--	Not recorded	Small
5	F	55	5/12	Positive	Small & large
6	F	37	5	Negative	Small
7	F	60	5	Positive	Small
8	F	35	2	Positive	Small
9	F	29	9	Positive	Small
10	F	50	15	Positive	Small
11	F	45	10	Positive	Small & large
12	F	50	4	Positive	Small & large
13	F	28	--	Positive	Small & large
14	F	50	1½	Positive	Small & large
15	F	50	7	Positive	Small & large
16	F	75	15	Positive	Small & large
17	F	50	4	Positive	Small & large
18	F	60	1	Positive	Small & large
19	F	32	5	Negative	Small & large
20	F	70	10	Positive	Small & large
21	F	70	--	Positive	Small & large
22	F	30	7	Positive	Small & large
23	M	42	10	Positive	Small & large

F = female; M = male.

In conclusion, Saudi patients with rheumatoid arthritis who live in the Asir region and who have no respiratory symptoms and normal chest x-ray studies may have abnormal spirometric and arterial blood gas values.

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Biotyping of Brucella Isolates

To the Editor: Biotyping of *Brucella* is useful in studying the reservoir host in various enzootic areas of brucellosis [1]. Various biotypes of *B. melitensis* are common in sheep in Southwest Asia and the Mediterranean countries and in goats in Latin America [2].

A variation in the biotypes of *Brucella* isolates from different geographical locations has been reported by different workers [1,2]. *B. abortus* biovar 1 was the most frequent biotype isolated in Africa and Indo-Pakistan, especially in the organized farms, while biovar 3 is more common in the traditional systems of husbandry with small herds, especially in the nomadic and seminomadic cattle herds.

Brucellosis is common in Saudi Arabia, yet no significant work has been done to identify the species and biotypes responsible. The only published work on this aspect was that of Corbel [3], who biotyped 53 isolates of *B. melitensis* from Saudi Arabia and found that 41% were biovar 1, 56% biovar 2, and 2% of biovar 3.

We present the findings of biotyping *Brucella* isolates from King Khalid University Hospital (KKUH), Riyadh. Between July 1987 and August 1989, 175 clinical isolates of *Brucella* were collected from patients presenting to KKUH. These organisms were cultured and biotyped according to their differential characteristics [4]. Briefly, isolates were examined for carbon dioxide requirements for growth and hydrogen sulfide production using lead acetate–impregnated filter paper strips over serum dextrose agar (SDA) slopes that were incubated at 37°C for 48 hr. Cultures were then tested for sensitivity to dyes (basic fuchsin and thionin), incorporated into SDA plates, and incubated at 37°C in an atmosphere supplemented with 10% carbon dioxide. Saline suspensions of the organism were tested for urease activity, and agglutination by monospecific anti-A, anti-M, and anti-R antisera. They were also tested for dissociation and lysis by bacteriophages (Tibilisi, Weybridge, Firenze, Rough and Berkeley). Reference strains (obtained from the Central Veterinary Laboratory, Weybridge, England) were used as controls. The results of discrimination tests are shown in Table 1. All 175 isolates were *B. melitensis;* 45% were biovar 1, 32% biovar 2, and 23% biovar 3.

Knowledge of the *Brucella* prevalent in Saudi Arabia may help to identify the source of importa-

TABLE 1. *Characteristics of Brucella species at KKUH.*

Biotype	CO_2 required	H_2 production	Growth on media containing		Agglutination with monospecific antisera			Lysis by phage at RTD					No. of strains
			Thionin	Fuchsin	A	M	R	Tb	Wb	Bk_2	Fi	R	
1	–	–	+	+	–	+	–	NL	NL	L	NL	NL	56 (32)
2	–	–	+	+	+	–	–	NL	NL	L	NL	NL	79 (45)
3	–	–	+	+	+	+	–	NL	NL	L	NL	NL	40 (23)
Total													175

Tb = Tibilisi; Wb = Weybridge; Bk_2 = Berkeley; Fi = Firenze, R = Rough; RTD = routine test dilution; NL = no lysis; L = lysis.

tion of brucellosis. This study illustrates the need for further studies on *Brucella* isolates from various animal reservoirs. Such data will have an important impact on control measures, especially the importation of livestock, as most infections in this country are likely to originate from imported animals.

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Mediastinal Aortic Aneurysm

To the Editor: New imaging techniques have brought about changes in the individual investigations and diagnostic procedures used for aneurysms. Dilatation of all components of the vessel wall is a known feature of aneurysms observed on radiological examinations. A number of vascular congenital malformations of the aorta and pulmonary artery appear as a mediastinal widening or mass on standard chest radiographs. They are usually discovered in the first year of life, with vascular rings and persistent aortic arch, as well as left ductus arteriosus as an incidental finding. Frequently these vascular abnormalities and their complications, such as thrombus formation, leak, true-false lumen, and dissecting flap, can be diagnosed only by computed tomography (CT) and magnetic resonance imaging (MRI). The total involvement of adjacent small branches can be confirmed by angiography prior to surgical intervention. With minimal enhancement the true lumen exhibits the same density as surrounding tissue, and thus escapes detection. Owing to the great diagnostic range of CT, the perivascular space can also be interpreted to represent a hematoma. Pericardial hematoma, vertebral body erosion, and calcification within a thrombus or the vessel wall can be more accurately localized with CT than with a scout view of the thorax. The major disadvantage of CT is that the transverse projection plane only allows cross-sectional images if the aorta runs obliquely to the image plane (kinking). This can therefore simulate a dilated lumen. The origin of the aortic arch and coronary artery cannot be imaged directly. CT scanning of the aorta always requires contrast enhancement.

A 50-year-old Sudanese man presented with a history of minimal dyspnea, common cold, and cough. Routine chest x-ray study (posteroanterior view) showed a large, well-defined lesion with peripheral calcification involving the mediastinum and displacing adjacent trachea and bronchus toward the contralateral side. It also revealed erosion of the posterolateral aspect of the sixth rib on the left side. The costophrenic and cardiophrenic angles were obliterated, with marked shift of the mediastinal structures to the right. Left lateral chest x-ray study and barium swallow was done, and barium swallow revealed the esophagus was slightly displaced anteriorly with no peristaltic movement visible over the barium column. The CT scan showed an extensive soft-tissue-density lesion, with calcification of the wall which was contiguous with the wall of the aortic arch (Figure 1). The lumen of the aorta was well visualized with smooth outlines and enhanced with a bolus contrast infusion. However, the adjacent soft tissue lesion did not show any enhancement. The wall surrounding the lesion showed calcification and enhancement. The lesion appeared to extend below the level of the subclavian artery to the carina. The descending part of the aorta was displaced toward the right and there was a massive pleural collection and thickening of the pleura (Figure 2). Following intravenous contrast enhancement, no extraluminal collection was seen; the

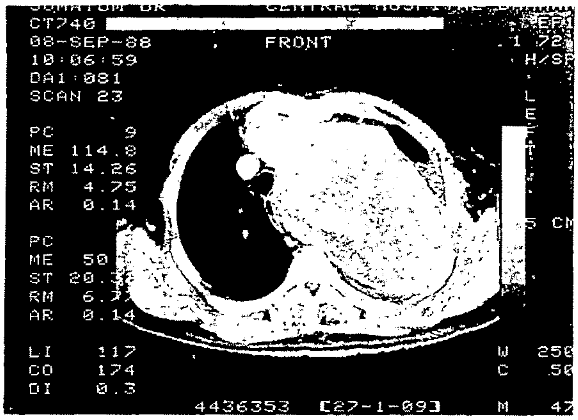

FIGURE 1. Large soft-tissue-density mass lesion with peripheral calcification which is contingunous with the wall of the aorta. The lesion is causing displacement of adjacent mediastinal structures and pressure erosion to the posterolateral part of the rib, along with minimal pleural effusion.

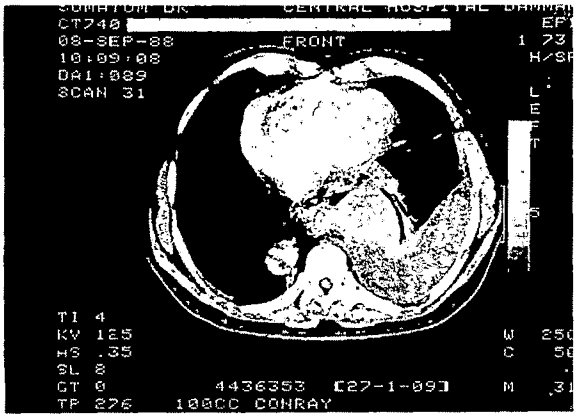

FIGURE 2. Massive pleural effusion on the left side of the descending aorta is tortuous and displaced toward the right.

lesion extended up to the lateral margin of the thorax, causing minimal erosion of the adjacent rib (pressure erosion). The trachea and mediastinal structures were displaced toward the right. The pulmonary trunk was well-opacified and normal in calibre with smooth outlines. Arch aortography showed a tortuous aorta below the carina and the intimal outlines of the aortic arch were smooth and uninterrupted, with a soft tissue lesion adjacent to the aorta causing contralateral displacement of mediastinal vascular and soft tissue structures. An aneurysm of the aortic arch containing multilaminated thrombus was confirmed on surgery.

In recent years, CT has become widely used in evaluating the thoracic aorta and has made the differentiation between an aortic aneurysm and mediastinal neoplasm easier. Recently MRI has also proved its value in imaging abnormalities of the thoracic aorta [1,2].

Conventional chest radiography may suggest the diagnosis, but further evaluation by angiography, CT, or MRI is generally required. CT is diagnostic for showing intimal or thrombus-related calcification, peripheral thrombus, and contrast-filled lumen. Demonstration of an attachment to the pulmonary artery on the chest film or on aortography is a highly specific finding, but may not be discernible in a very large aneurysm. CT is also useful for distinguishing this entity from the ductus diverticulum, which is characteristically not associated with mural thrombus. In light of the recent review describing normal variant ductus diverticulum (present in 90% of thoracic aortograms), some large enough to be present as a distinct entity on CT [3,4], patients must be evaluated carefully and pathological anomalies identified using thorough radiological investigations.

Calcification within or in the lumen wall is a frequent finding, making it difficult to differentiate between an aneurysm and a solid tumor invading the aortic arch, particularly when the tumor grows around the aortic arch like a cuff [5]. The most common configuration is a complete ring of thrombus with surrounding calcification, which is seen in the CT scans of 83 to 100% of the cases [6,7]. However, 17% of the cases have been confused with infiltrating solid mediastinal tumors. Gorden et al [personal communication] have observed only one case in which the scan showed an extensive soft-tissue mass lesion in the mediastinum, with pleural effusion.

Fomon et al [9] have shown that the potential for rupture of an aortic aneurysm is directly related to its wall and its size. Aneurysms less than 5 cm in diameter, if untreated, have an approximately 10% chance of rupturing. Most thoracic aortic aneurysms can be suspected from chest radiographs. The most common radiographic finding is a mediastinal mass or an enlarged segment of the aorta with calcification in the wall. Displacement and, less frequently, compression of the esophagus, trachea, and bronchi may be visible on radiographs. Erosion of the thoracic vertebrae and posterior ribs can also occur, but is uncommon.

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Brain Death Protocol: Update

To the Editor: The brain death protocol mentioned in my article on cadaveric organ donation [1] has recently been revised by the National Kidney Foundation. The revised stance is that the clinical assessment of brain death may be initiated six hours after the initial insult and repeated after six instead of 24 hours. Only one isoelectric electroencephalogram or cerebral angiogram is needed to confirm brain death. It is hoped that these measures will lead to greater donor stability and healthy organs for transplantation.

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Symposium Abstracts

RECENT ADVANCES IN INFECTIOUS DISEASES

Sponsored by the Joint Board for Postgraduate Medical Education
King Fahad National Guard Hospital, Riyadh
25-26 Shawwal 1410
(20-21 May 1990)

EPIDEMIOLOGICAL INVESTIGATIONS OF A PATIENT WITH DISSEMINATED TUBERCULOSIS, CUTANEOUS LEISHMANIASIS AND AIDS, MY Khan, S Al-Mahmood, King Fahad National Guard Hospital, Riyadh

A 58-year-old Saudi male patient was admitted in 1989 with a left neck mass, which on biopsy showed evidence of tuberculosis. Disseminated tuberculosis developed while the patient was receiving anti-TB therapy. He was found to be positive for human immunodeficiency virus (HIV) antibody. He was markedly immunosuppressed with cd 4 cell count of 21/μl and a cd 4/cd 8 ratio of 0.06. Numerous skin lesions appeared, which on biopsy and culture proved to be due to *Leishmania* infection. The patient eventually died from an overwhelming HIV infection. He had no known risk factors. His second wife, with whom the patient was living, tested positive for HIV antibody. On further investigation, it was discovered that she had received two units of blood for nutritional anemia in 1983, obtained from two expatriate donors. One of the donors was subsequently found and tested positive for HIV antibody. The wife's three children were screened for HIV antibody. One child was born before the positive transfusion but two children were born after the transfusion positive for HIV antibody. This case demonstrates that patients with AIDS may suffer disseminated infections with organisms endemic in a geographic area. Furthermore, a grave risk is posed to the family members of the HIV-infected blood transfusion recipients.

TREATMENT OF CYTOMEGALOVIRUS INFECTION, TC Merigan, Stanford University School of Medicine, Stanford, California, U.S.A.

In recent years, because of the increasing iatrogenic use of immunosuppression, including the graft maintenance and cancer chemotherapy as well as the occurrence of AIDS, physicians have been seeing increasing cases of cytomegalovirus-caused disease. Although drugs initially tried as therapy were not reproducibly effective, in the last few years, two agents have appeared with clear-cut benefits. These include gancyclovir (DHPG) and Foscarnet (phosphonoformic acid). These agents reproducibly suppress viuria and viremia. Gancyclovir has shown widespread activity against cytomegalovirus (CMV) retinitis, for which it has been licensed for use in the United States. It is also being utilized for CMV colitis and pneumonia. It is the first agent to show any effect against established CMV pneumonia in bone marrow transplants when given in conjunction with immune serum globulin. Recently, the use of prolonged therapy in resistant mutants, where the changes are located in the viral DNA polymerase gene, has revealed which are sensitive in vitro and clinically responsive to Foscarnet. Both these agents unfortunately suffer from a lack of bioavailability when given orally. Therefore a search for orally active alternatives is under way with several interesting candidate drugs under study. These agents as well as newer diagnostic methodology were discussed.

INCIDENCE AND ETIOLOGY OF BACTERIAL INDUCED DIARRHEA AT A MAJOR REFERRAL CENTER IN SAUDI ARABIA, SMH Qadri, HT Tufenkeji, K Al-Qatary, King Faisal Specialist Hospital and Research Centre, Riyadh

Infectious diarrhea is the largest single cause of morbidity and mortality in the world. Over 200 million people worldwide suffer from it in any given 24-hour period, with 3 to 10 million deaths each year in developing countries alone. Bacteria, viruses, and protozoan parasites are the most common causes. Among bacteria, *Salmonella, Shigella, Campylobacter, Escherichia coli* (enterotoxigenic, enteropathogenic, enteroinvasive, enterohemolytic, and enteroadherent), and *Vibrio* are the most important diarrhea-causing agents. To determine the incidence and etiology of bacteria-induced diarrhea, we retrospectively examined the laboratory records of 19,437 patients, for whom 34,856 stool specimens were available, during a 5-year period (1985-1989) at a major tertiary care referral hospital in Saudi Arabia. Bacterial pathogens were isolated from 1426 (7.3%) patients, with *Salmonella* the most frequent (3.8%), followed by *Campylobacter* (2.0%), *Shigella* (1.1%), and *Aeromonas hydrophila* (0.34%). *Salmonella* serogroups B and C and *Shigella* B and D constituted most of the isolates in these two groups, respectively. Major clinical symptoms of bacterial gastroenteritis included mild to moderate diarrhea, abdominal discomfort, tenesmus, vomiting, fever, and dehydration. Bloody diarrhea was more common in patients with shigellosis (32%) than in those with other bacteria. Stool specimens from 80% of patients with *Shigella* gastroenteritis had leukocytes, as compared with 38% of those with *Salmonella* or *Campylobacter.*

AIDS–THERAPY OF HIV INFECTIONS, TC Merigan, Stanford University School of Medicine, Stanford, California, U.S.A.

It is clear that new therapeutic strategies must be developed for all stages of HIV infection and disease. As with most infectious microorganisms, drug side effects and microbial resistance will limit the impact of any one drug to only certain selected clinical disease settings and patients, and for limited periods in the natural course of the infection. Fortunately, at this time, more intense efforts and funding have been directed at controlling this organism than toward any other disease entity in history. As a result, many novel and rationally developed chemical and biological therapies are being explored. Both receptor-based and posttranslational agents as well as several new reverse transcriptase-directed inhibitors are in Phase 1 and 2 testing. An approach to establishing the best dose, route, and schedule of new agents is being developed, based on surrogate markers, namely serum P24 and CD4+ cells. The latter are also being utilized for evaluation of the optimum dosage and the role of each component given in combination therapy. Combination therapy should diminish the emergence of drug resistance and allow dose reduction to lessen both the short- and long-term occurrence of side effects. Unfortunately, one of the most interesting combinations of two agents with different mechanisms of action (AZT and αIFN) is complicated by the fact that both agents show hematotoxicity. Then, as is currently under way within the U.S. AIDS Clinical Trials Group, only very careful and complete probing of the full response surface will reveal the optimum combination. The use of biologics, like interleukin-2, is also complicated, as one must approach the organism through host responses, hence their use can be very specific to the stage of disease. Yet, in all these areas, progress is being made and will be summarized in this presentation.

BACTEREMIA IN YOUNG SAUDI CHILDREN, S Said, M Al-Shaalan, H Yaish, King Fahad National Guard Hospital, Riyadh

We studied retrospectively the clinical presentation of 74 Saudi children who were admitted to KFNGH between 3 and 24 months of age and who were found to have a positive blood culture during the initial investigation of their febrile illness. Our study was designed to evaluate the predictive values of certain parameters in identifying patients at high risk of bacteremia. The blood cultures in 31/74 children (14M; 17F) were considered contaminated by nonpathogenic organisms and thus were used as controls for comparison with 43 children (30M; 13F) with documented bacteremia. We found that *Hemophilus influenzae* and streptococcal pneumonia were the most commonly encountered organisms in the population, with 16 patients (37%) for each. *S. aureus* was found in 16%, and less frequently, *K. pneumonia, Salmonella,* and *N. meningitides.* The mean rectal temperature was 39.5°C compared with 38.4°C in controls. The difference is statistically significant at $P < 0.001$. Even though the Hbg level in the patients was lower than that in controls (9.7 vs 10.7 gm/dl%), the difference was not significant. The total WBC of $\geq$ 15,000/mm^3 was observed in 29 patients (67%), compared with only 6 controls (19%). Similarly, an absolute PMN count of $\geq$ 10,000/mm^3 was encountered in 24 patients (62%) in contrast to five controls (16%). The differences for both parameters were statistically significant at $P < 0.02$ and < 0.0001, respectively. In contrast, an absolute band count of $\geq$ 500/mm^3 was seen in 33 of 36 patients (91%), compared with seven of 20 controls (35%). The difference was significant, however, at $P = 0.05$. We concluded that a rectal temperature of $\geq$ 39.5°C and a total WBC $\geq$ 15,000/mm^3 with an absolute PMN count of $\geq$ 10,000/mm^3 and an absolute band of $\geq$ 500/mm^3 in a child of 3 to 24 months of age represents a good predictor of bacteremia.

BACTERIAL MENINGITIS IN CHILDREN AT KFNGH, RIYADH, SAUDI ARABIA, A Kagalwalla, H Yaish, King Fahad National Guard Hospital, Riyadh

The medical records of 37 consecutive children with culture-proven bacterial meningitis were reviewed retrospectively in order to study the epidemiology, bacteriology, treatment, and complications of this potentially lethal disease. There were 15 males and 22 females (age range, 1 to 144 months; mean age, 15 months). Thirty-one patients (88%) were under the age of 18 months. Seventy-seven percent of the patients presented during the cooler months (November to April), with a peak incidence during December and January. *Hemophilus influenzae* was isolated from the CSF of 66% of the patients, *Streptococcus pneumoniae* in 23%, and *Neisseria meningitidis* in 9%. Blood cultures were positive for the same organism in 77% of the patients. The highest correlation between blood and CSF cultures occurred in 96% of patients with *Hemophilus influenzae* meningitis. All but one *Hemophilus influenzae* isolate were sensitive to ampicillin. There were no isolates resistant to chloramphenicol. *Streptococcus pneumoniae* and *Neisseria meningitidis* were all sensitive to penicillin. Fever was the presenting symptom in 66%, followed by seizures in 29%. Other symptoms included vomiting (69%), reluctance to eat (43%), and diarrhea (23%). The duration of the symptoms prior to presentation ranged from one to 7 days (mean, 3.4 days). A history of previous antibiotic use was documented in 31% of the patients. Ampicillin and chloramphenicol were the initial antibiotics used in all patients until culture and sensitivity results were available. One child with *Hemophilus influenzae* meningitis died within 48 hours despite aggressive management with appropriate antibiotics. Hydrocephalus requiring ventriculoperitoneal shunt occurred in one child. Deafness was present in 5 of the 10 who returned for audiological assessment.

NEONATAL SEPSIS IN THE NEONATAL INTENSIVE CARE UNIT, GS Ahmed, J Ellis, S Khan, AR Abu-Taleb, H Yaish, Department of Pediatrics, King Fahad National Guard Hospital, Riyadh

Neonatal septicemia is a significant cause of neonatal mortality and morbidity. The rate of infection differs among institutions and countries. There are shifting patterns of causative organisms, hence it is important that each institution review the pattern of infection in their nurseries. During a 2-year period (July 1987 to June 1989) the incidence of neonatal sepsis (documented by positive blood cultures) was found to be 0.22% (N = 16). *E. coli* and *Klebsiella pneumoniae* accounted for 37.5% of the episodes. A variety of other organisms were responsible for the remaining cases of sepsis. Meningitis was associated with sepsis in 12% and with localization of infection at other sites in 25% of the infants. The most common presenting signs were lethargy and tachypnea. Other signs including hypo- and hyperthermia, apnea, jaundice, and abdominal distention were also encountered. Total leukocyte count was less than 5,000 cells/mm^3 in 25% of the cases while a bands-to-segmental neutrophils ratio of greater than 0.2 was noted in more than 60% of patients. Except for staphylococci, all organisms were sensitive to ampicillin or gentamicin, which were the initial antibiotics given. The overall incidence of mortality associated with septicemia was 19%. All were full-term infants referred from outside. The fact that we had no deaths among the in-born babies in this study could be attributed to the advent of neonatal intensive care facilities and to the increased awareness on the part of medical personnel. Minor changes in infants' conditions such as subtle fluctuations in the level of activity or respiratory status are picked up and managed promptly. We conclude that a variety of organisms can produce sepsis in the newborn. Early diagnosis and prompt management can lead to a favorable outcome.

EVALUATION OF PERCUTANEOUS CENTRAL VENOUS SILASTIC CATHETERIZATION IN NEWBORNS AND INFANTS, AR Abu-Taleb, J Ellis, S Khan, GS Ahmed, H Yaish, Department of Pediatrics, King Fahad National Guard Hospital, Riyadh

Prolonged parenteral nutritrion has become a cornerstone of modern medical management in sick premature infants. With the increased survival of extremely low-birth-weight infants, efforts should be directed toward reducing morbidity. Often there is a need for central venous access in these patients when oral feedings are contraindicated or not tolerated. However, the use of surgically placed Broviac catheters has been associated with a high rate of complications. We evaluated the use of percutaneous central venous Silastic catheterization in 29 patients. There were 22 premature and seven full-term infants. At the time of catheterization, 14 weighed less than 1,500 gm and 8 were less than 1,000 gm. The mean duration of catheterization was 21.4 days (range, 6 to 71 days). Eighteen (62%) were removed electively. There was one case (3.45%) of bacteremia caused by *Streptococcus* species. Clinically three patients (10.3%) were suspected to have sepsis; however, they did not have bacteremia and cultures of the catheter tips were negative. The overall incidence of mechanical complications was 24.1% (7/29). In conclusion, percutaneous central venous catheters can be used safely and effectively in newborns for prolonged administration of total parenteral nutrition.

PHAGOCYTE FUNCTIONS OF PERIPHERAL BLOOD MONOCYTES IN BRUCELLOSIS, AK Al-Aska, A Al-Tuwaijry, K Halim, IO Al-Orainey, College of Medicine, King Saud University, Riyadh

One of the principal functions of phagocytic cells is to ingest and destroy microorganisms. The ability of the monocyte macrophage system to destroy target pathogens like *Brucella* depends, in part, on its capacity to generate toxic oxygen products (respiratory burst). There is growing evidence that incompetence in the monocyte-macrophage system could be responsible for the chronicity of brucellosis. In order to assess the capacity to generate respiratory burst, we examined oxidative metabolites from the monocytes of patients with brucellosis. For this purpose, peripheral blood monocytes were isolated for chemiluminiscence assay from 56 patients with brucellosis and 18 normal controls. Patients were divided according to their clinical presentation into noncomplicated, complicated, and post-treatment groups. The complicated group showed a significant reduction for the maximum chemiluminiscence peak ($P < 0.05$) and integral ($P < 0.01$). Conversely, the control and noncomplicated groups demonstrated a significant reduction in integral ($P < 0.05$) only. The pretreatment group (complicated and noncomplicated) showed a significant reduction as compared with controls in both the integral and time-to-peak chemiluminiscence ($P < 0.05$). Another aspect of this study was monocyte antibody–dependent cellular cytotoxicity. Monocytes from 21 patients and 16 normal controls from the same study of the population were available for the study of antibody-dependent cellular cytotoxicity. Killing ability was significantly reduced ($P < 0.05$) in all patient groups at 24 hours (incubation with red blood cells).

PHAGOCYTIC FUNCTIONS OF POLYMORPHONUCLEAR LEUKOCYTES (PMN) IN BRUCELLOSIS, AK Al-Aska, A Al-Tuwaijry, K Halim, IO Al-Orainey, College of Medicine, King Saud University, Riyadh

Ingestion and killing by phagocytic cells is one of the early nonspecific defense mechanisms against *Brucella*. Degradation of the microorganism is associated with an increased consumption of oxygen that leads to the appearance of toxic oxygen products. The level of these toxic products, as a result of respiratory burst, correlates with the antibacterial activity of phagocytes. Inability to induce respiratory burst may be one of the factors influencing the survival of *Brucella* in PMN during the early stage of infection. Therefore, we examined the oxidative metabolites of PMNs of patients with brucellosis. Isolated PMNs from heparinized venous blood of 56 patients with brucellosis and 18 normal controls were loaded into an LKB luminometer for chemiluminiscence assay. (The isolation method of PMNs and performance of the assay have been previously described.) Patients were divided into noncomplicated, complicated, and post-treatment groups according to their clinical presentation. Compared to normal controls, PMNs isolated from brucellosis patients showed no significant difference ($P > 0.05$) in chemiluminiscence maximum peak or the integral. However, after the exclusion of patients exhibiting abnormally high or low values, a significant reduction in maximum chemiluminiscence peak and integral ($P < 0.05$) for the complicated patient group and a significant reduction of time to peak for the noncomplicated group were found.

RAPID DIAGNOSIS OF STREPTOCOCCAL PHARYNGITIS, BH Qureshi, Central Lab and Blood Bank, Riyadh

Demonstration of group "A" surface antigen of group "A" beta-hemolytic *Streptococcus* by the technique of passive agglutination has made it possible to diagnose streptococcal throat infection easily and rapidly to allow for specific therapy. We extracted the group "A" antigen of *Streptococcus* from the throat swab specimen by the commercially available reagent from Wellcome Diagnostics, then it was detected by the latex particles coated with antibody against group "A" antigen. This method was compared with the culture technique in 200 patients attending the outpatient clinic at Central Hospital and Maternity & Children's Hospital, Riyadh. The study indicated that the passive agglutination technique for the detection of "A" streptococcus antigen in throat swabs is rapid and simple, and is 100% sensitive and 97.9% specific when compared with the bacterial culture method.

CONTROL OF METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS OUTBREAK AT A NEONATAL INTENSIVE CARE UNIT, Q Haddad, OB Basit, E Sobayo, Security Forces Hospital, Riyadh

Security Forces Hospital, Phase II, is one of the newest hospitals in Riyadh. Within less than two years, a major expansion program of from 120-bed occupancy to nearly 350 beds was carried out. Neonatal intensive care unit (NICU) admissions increased by 30% during 1409H without significant change in the NICU construction, space allocation, or nursing staff.

Methicillin-resistant *Staphylococcus aureus* (MRSA) was described soon after methicillin became available for clinical use in 1960. Outbreaks of MRSA have been reported since 1969. During December 1989 through January 1990, sixteen (16) cases of MRSA were identified. MRSA probably contributed to the death of two patients. A detailed epidemiological study was carried out to locate the source of the outbreak. The likely source was a phenolic disinfectant (Wexcide) which was utilized longer than the recommended time limit. Closure of the unit for further admissions was not feasible. Guidelines to control this outbreak including the use of mupirocin, creating an isolation room, increasing nursing staff, and controlling the traffic were the main factors in controlling the outbreak.

EPIDEMIOLOGY OF BRUCELLOSIS IN SAUDI ARABIA, A Al-Nasser, A Al-Aska, S Alballa, IA Al-Mofleh, M Al-Sukait, OS Hassan, Department of Community Medicine and Department of Medicine, College of Medicine, King Saud University, Riyadh

Purpose: To determine the prevalence of brucellosis in Saudi Arabia and to study the prevalence and importance of relevant risk factors in the epidemiology of the disease. *Methods:* A total of 23,000 stratified random samples were studied. A questionnaire was filled out which included relevant risk factors.. Serum from all individuals was also analyzed by the microplate agglutination test. Positive cases were further analyzed using the tube agglutination test and 2-mercaptoethanol test. Active diseases were diagnosed with a tube agglutination titer of 1:160 and the presence of symptoms compatible with brucellosis. Cases with a tube agglutination of less than 1:160 and with signs and symptoms compatible with brucellosis were diagnosed as active disease if the 2-mercaptoethanol test were positive at a titer of 1:140 or more. *Results:* Exposure rate was determined by the microplate tube agglutination test (35%). Active disease was diagnosed in 2% of the samples selected. A highly significant association was found between exposure to animal and animal products and a positive microplate. The most common presenting features of brucellosis in Saudi Arabia are discussed in relation to other epidemiological variables. This project was sponsored and funded by the Ministry of Health, Riyadh.

SEROEPIDEMIOLOGY OF HUMAN BRUCELLOSIS, AK Al-Aska, A Al-Tuwaijry, IO Al-Orainey, K Halim, O Sheick, College of Medicine, King Saud University, Riyadh

Following the recognition of human brucellosis as a cause of significant morbidity in the Kingdom, a community-based cross-sectional survey was conducted in Al-Kharj, a small city about 80 km east of Riyadh and with an estimated population of 68,000, to determine the prevalence of serological reactivity against *Brucella* antibodies and the factors that play a major role in the transmission of the microorganism. In a stratified random sampling, 400 families (comprising 3,200 subjects) from 20 clusters were interviewed according to a standardized written form and then blood samples were obtained. All sera were initially screened for *Brucella* antibodies by the microplate agglutination test and only the positive reactors were further investigated by the standard tube agglutination test. Since the microplate test was found to be highly sensitive and included cross-reacting antibodies at lower dilutions (false-positives), a titer of ≥ 1:160 by the microplate agglutination test was found to represent specific *Brucella* antibodies. Antibodies against *Brucella* were present in 13.9% of the sera, indicating a high exposure rate of *Brucella* antigens in this community. This finding agrees with the observation that a high percentage of household animals in Al-Kharj had antibodies against *Brucella*. The relative importance of the risk factors in the transmission of *Brucella* organisms is discussed.

BRUCELLOSIS IN SAUDI FEMALES, AA Sabah, YM Hussain, MZ Khawagy, Internal Medicine Department, Riyadh Central Hospital, Riyadh

In 1408H, over a 3-month period, 129 consecutive cases of brucellosis were diagnosed in Saudi females at the female outpatient medical clinic at Riyadh Central Hospital. Age ranged from 12 to 70 years. 113 (87.6%) of the patients gave a positive history of raw milk ingestion, mostly from sheep; 13 (10%) gave a positive history of home slaughtering of sheep only; 2 patients (1.5%) gave a history of animal contact alone. The remaining patient had no history of exposure but her husband suffered from brucellosis. The main presenting symptoms were: fever (79.5%), headache (72.4%), generalized arthralgia (65.3%), sweating (65.3%), chills (63.8%), low back pain (34.6%), abdominal pain (27.5%), loss of appetite (25.5%), lassitude (17.2%), myalgia (14.2%), nonarthralgia (7.9%). Spinal involvement was present in 15% of the cases, 3/4 of whom were suffering from chronic brucellosis. 78.2% of the patients with a titer ≥ 1:640 were under 40 years of age, presenting with acute/subacute illness. Titers ≤ 1:320 were found in 2/3 of chronic cases. 32/35 responded to combination of streptomycin and tetracycline, 17/21 to streptomycin and septrin, 38/43 tetracycaline and septrin, 26/26 to a combination of rifampicin with tetracycline or septrin, 26/26 to a combination of rifampicin with tetracycline or septrin. All 12 resistant cases responded to the last regimen. Clinical course and modes of therapy were discussed.

OUTCOME OF BRUCELLA INFECTION IN PREGNANCY, MY Khan, F Kiel, JP Dery, King Fahad National Guard Hospital, Riyadh

This report summarizes our experience with 42 pregnant women among 332 inpatients with brucellosis observed over a 6-year period. Diagnosis was based on clinical features and a *Brucella* titer of 1:320 or greater. Blood cultures were positive for *Brucella* species in 47%. *B. melitensis* was the most frequent species cultured from these patients. The overall abortion rate was 50%. There was no significant difference in abortion incidence between bacteremic and nonbacteremic cases. Twelve patients presented with *Brucella* infection in the third trimester. Two received co-trimoxazole (TMP/SMZ) and one was given TMP/SMZ plus rifampin for over four weeks before delivery. The other nine were symptomatic at the time of delivery and received anti-*Brucella* therapy after delivery. All twelve delivered live babies (two prematurely). The remaining thirty patients were diagnosed in the first (9 patients) and second (21 patients) trimesters. Twenty of these patients, presenting mainly with vaginal bleeding, aborted without receiving prior anti-*Brucella* treatment. The remaining 10 patients mainly presented with fever and arthralgia, and were given anti-*Brucella* treatment. Eight of these received TMP/SMZ and two were given TMP/SMZ plus rifampin for over 4 weeks. Nine subsequently delivered normally, whereas only one aborted. In conclusion, brucellosis in pregnancy induces abortion in a high proportion of cases. Abortions were mainly in the first and second trimesters of pregnancy. *Brucella* infection did not show ill effects in late pregnancy even when patients were bacteremic. Anti-*Brucella* therapy (TMP/SMZ with or without rifampin) given early in pregnancy appears to prevent abortion.

BIOTYPING OF BRUCELLA ISOLATES FROM SAUDI ARABIA, MEM Eltigani, NS Saeed, AM Kambal, IB Al-Orieny, King Khalid University Hospital, Riyadh

There are four species of *Brucella* that may infect humans: *B. abortus, B. melitensis, B. suis,* and *B. canis*. Although brucellosis is common in Saudi Arabia, the actual prevalence of species causing the disease is not well known. The objective of the study was to biotype and phage-type *Brucella* isolates at KKUH and to correlate specific biotypes with the clinical presentation. 175 strains of *Brucella* collected at KKUH over a period of three years were biotyped using the following procedures: CO_2 requirement for growth, H_2S production, growth on media containing thionin and basic fuchsin dyes, and agglutination with monospecific antisera (A, M, and R). The strains were also phage-typed (at RTD) using the following phage: Tb, Wb, BK_2, and F_1. All strains did not require supplementing CO_2 for growth and did not produce H_2S. They hydrolysed urea and grew on media containing thionin and fuchsin dyes. All strains were lysed only by BK_2 phage at RTD. These tests together with the reaction of the isolates with mono-specific antisera led us to the conclusion that all isolates were *B. melitensis.*

COMPUTED TOMOGRAPHY IN THE MANAGEMENT OF LIVER HYDATIDS, DB Lewall, King Fahad National Guard Hospital, Riyadh

Liver hydatids can be evaluated by ultrasound (US), computed tomography (CT), and nuclear magnetic resonance imaging (MR). CT is generally more available than MR, is easier to interpret, and displays anatomic relationships more clearly than US. We present our experience with 45 patients with hydatid cysts of the liver treated at the King Fahad Hospital, augmented by prior experience with 59 patients at another institution. With CT it is possible to study the progression of lesions from simple Type I cysts, through complex Type II lesions with daughter cysts with or without matrix, to dead Type III lesions. CT also makes it possible for us to diagnose rupture and complications of rupture such as biliary obstruction, which usually causes cholangitis. An understanding of the three mechanisms of rupture clarifies the complications which result from rupture. CT analysis of hydatids is helpful in planning the surgical approach, and in assessing the feasibility of purely medical management. Although the last word on medical management of hydatids has not been written, CT does enable us to identify certain situations in which purely medical management could be dangerous.

COMPARATIVE IN VITRO ACTIVITIES OF QUINOLONES AND OTHER SELECTED ANTIMICROBIAL AGENTS AGAINST *BRUCELLA MELITENSIS,* MY Khan, M Dizon, FW Kiel, King Fahad National Guard Hospital, Riyadh

Brucellae are intracellular pathogens and reside mainly in phagocytic cells, where they may remain protected from antibodies and certain antimicrobial agents. Quinolones appear to achieve intracellular concentrations in phagocytic cells significantly in excess of extracellular concentrations. This ability makes these antimicrobial agents suitable for use against infections caused by intracellular bacteria. The in vitro activities of three quinolones (ofloxacin, difloxacin, and ciprofloxacin) were compared with those of trimethoprim-sulfamethoxazole, streptomycin, tetracycline, and rifampin against 47 *Brucella melitensis* strains. Ofloxacin was the most active of the test antimicrobial agents. It inhibited 90% of *B. melitensis* strains at a concentration of 0.02 μg/ml. In comparison, difloxacin and ciprofloxacin inhibited 90% of strains at a concentration of 1.25 μg/ml. Our in vitro results demonstrate that these three quinolones are quite active against *B. melitensis,* which is the most common species causing brucellosis in the Middle East. However, initial clinical trials of ciprofloxacin have not shown satisfactory results. Ofloxacin and difloxacin in vitro activities compared favorably with those of antimicrobial agents currently in use for the treatment of brucellosis. In view the satisfactory in vitro activities of these two quinolones, clinical trials to verify their efficacy in treating brucellosis are warranted.

THE DEVELOPMENT AND USE OF MODERN MOLECULAR BIOLOGY TECHNIQUES IN THE DIAGNOSIS OF INFECTIOUS DISEASES, RG Marusyk, Department of Medical Microbiology and Infectious Diseases and Research and Development Division, Provincial Laboratory of Public Health, Faculty of Medicine, University of Alberta, Edmonton, Alberta, Canada

Within a relatively short time, diagnostic methodologies have undergone an evolution akin to the original discoveries of the basic concepts of molecular biology. It will soon be possible to routinely and definitively diagnose certain infectious diseases and with great rapidity, e.g., Epstein-Barr virus infection and *Mycobaterium* infection. The greatest thrust in this area has occurred in the field of nucleic acic hybridization utilizing the polymerase chain reaction (PCR) or similar methodologies. With these new methods, under optimal conditions, the presence of a virus, for example, can be detected in transplant tissue within a matter of hours. These techniques are not limited to the detection of microbial genomic material, but can also be used to detect the presence or absence of a multitude of genomic material of medical and clinical importance, e.g. DNA may be analyzed for the presence of a specific mutation or polymorphism. A number of recently introduced commercial diagnostic tests are dependent on nucleic-acid-based technology. Improvements in the PCR/hybridization method have already been reported and show promise of further enhancement of the rapidity and specificity obtained. An overview of this important new area of diagnostics will be presented and will include a description, including the pitfalls inherent in the methods, of several of the more promising techniques.

ECHINOCOCCOSIS-HYDATID DISEASE: LESSONS FROM EXPERIENCE WITH 59 PATIENTS, JW Schaefer, MY Khan, M Al-Johani, King Fahad National Guard Hospital, Riyadh

Echinococcal hydatid disease is endemic in Middle Eastern countries, including Saudi Arabia. This study is based on a review of 59 cases seen at the King Fahad National Guard Hospital over a seven-year period. The diagnosis was based on characteristic appearances on ultrasonic (US) and/or computed tomographic (CT) images. There were 23 men and 36 women in this series, ranging from 12 to 80 years of age. Thirty-five (59%) had only one identifiable cyst. The remaining 24 patients had more than one cyst. The frequency of organ involvement with echinococcal cysts was as follows: liver, 45; spleen, 7; lung, 4; kidney, 3; retroperitoneal, 3; soft tissues; 3, mesentery, 2; and pericardial, 1. Chronic abdominal discomfort, often associated with a palpable mass, was the main presenting finding. The indirect hemagglutination serological test results were elevated in 18 of 35 (54%) patients tested. The eosinophil count was elevated in 16 (24%) patients. Thirty-seven patients with symptomatic cysts were operated on. Most often conservative extraction of the inner embryonic membranes proved effective, but cysts not extensively involving vital structures were totally excised. Citrimide was the local scolicidal agent of choice, while albendazole is considered beneficial for systemic chemotherapy. Elective surgery in 30 patients was safe. Urgent surgery in seven patients with acute complications from cyst rupture had high morbidity and mortality (four deaths).

HYDATID DISEASE IN SAUDI CHILDREN: EPIDEMIOLOGY AND MANAGEMENT, FM Mousa, HM Hassab, AM El-Sowailim, IH Ghani, K Gangadharan, Department of Pediatrics and Pediatric Surgery, Maternity and Children's Hospital, Riyadh

A retrospective study was conducted of all patients admitted to Maternity and Children's Hospital–Riyadh with a final diagnosis of hydatid disease. Over a period of 4 years (1985 to 1989) 24 children were seen. The mean age was 6.7 years (range, 3.2–12.4). Fourteen (58.4%) were males and 10 (41.6%) were females. Twenty (83.4%) were Saudis and 4 (16.6%) were non-Saudis (2 Palestinians, 2 Yemenis). Eleven (45.8%) were from the northern province, 7 (29.2%) from the south, and 6 (25%) from the central province. The liver was involved with unilocular cyst or multilocular cysts in 12 (50%) subjects. Five (20.7%) had lung involvement and three (12.5%) had both hepatic and alveolar implantation. Other sites found to be involved were: the left kidney (4.2%), pelvic tissues (4.2%), and retroperitoneal and subcutaneous tissues (8.4%). Abdominal enlargement, pain, fever, recurrent chest infection, and jaundice were the main clinical presentation. Marked eosinophilia (greater than 6%) was seen in 38%, and Casoni test was positive in only 11 (45.8%) patients. Mebendazol (30 mg/kg/day for 3–6 weeks) proved ineffective. Surgery was done for all cases. Endocystectomy, pancystectomy, and/or pericystectomy were the procedures done, depending on the size and site of the cyst. Five (20.8%) patients developed post-operative biliary fistula; all responded to conservative treatment. Hydatid disease is not uncommon among Saudi children, particularly in sheep-rearing areas. Chemotherapy is not curative and surgery remains the treatment of choice.

RETROSPECTIVE STUDY OF ISOLATES FROM HIGH VAGINAL SWABS (HVS), AN Boralkar, F Agbemadzo, A Arora, T Dasmunshi, MH Hassonah, Prince Salman Bin Abdulaziz Hospital, Riyadh

We have investigated a total of 2,194 high vaginal swabs (HVS) from clinically suspected cases of vaginitis during June 1988 to September 1989. HVS were processed for wet smear examination, culture, and sensitivity. For culture, blood agar (BA), chocolate agar, MacConkey agar, Sabouraud (SAB) agar, and Thayer Martin (TM) agar (Saudi Prepared Media Ltd) were used. Antibiotic sensitivity test was carried out by the disc diffusion method on Mueller-Hinton agar, BA for β hemolytic streptococci, and TM agar for *Neisseria gonorrhoeae*. Wet smears were examined for pus cells, clue cells, bacteria, fungal elements, and *Trichomonas vaginalis* (TV). TV was seen in < 1% cases. Yeast form and pseudohyphae showed good correlation with cultural findings on SAB agar. Commensal flora isolated on culture were not reported when wet smear findings were within normal limits. Of 611 (27.8%) positive cases, the most common isolate was *Candida albicans* (48.4%), confirmed by germ tube formation and agglutination with specific antisera (DIFCO). Pathogens isolated were *Staphylococci aureus* (5.6%), *Proteus* sp. (4.1%), Streptococci pyogenes (3.4%), *Pseudomonas aeruginosa* (2.1%), and *Neisseria gonorrhoeae* (0.7%). Other normal flora consistently isolated in patients with increased pus cells included *Streptococcus agalactiae* (24.2%), *Klebsiella pneumoniae* (6.5%), and *Escherichia coli* (4.9%). Their etiological role is very difficult to prove. Polymicrobial growth was seen in eight cases. The only striking feature in the antibiotic sensitivity test was resistance of *S. agalactiae* to cotrimoxazole (> 90%) on BA by the Kirby Bauer method using Mastering-S (MAST LAB, U.K.). Correlation of clinical findings, wet smear, and culture is necessary. In the cases where the causative agent was not found, increased physiological discharge or excessive cleaning with chemicals might have been responsible for clinical symptoms. Gardnerella and Chlamydia were not included in the study.

BACTEREMIA IN A TEACHING HOSPITAL IN SAUDI ARABIA, IO Al-Orainey, MS Al-Nasser, ES Saeed, MN Chowdhry, College of Medicine, King Saud University, Riyadh

During one year, 270 episodes of bacteremia were documented at King Khalid University Hospital, Riyadh, with an incidence of 11.7 cases per 1000 admissions. One hundred seventeen of these were hospital-acquired bacteremias. Over 70% of the isolates were gram-negative organisms. *Brucella* accounted for 24% of the isolates, and all were acquired in the community. The other common gram-negative isolates were *E. coli,* and *Klebsiella* sp. *Staphylococcus aureus* was the most frequent gram-positive isolate. The source of infection was identified in over 75% of the patients with non-*Brucella* isolates. The urinary and respiratory tracts were the most common sources of bacteremia. The overall mortality in this series was 15% and was more common among patients with nosocomial bacteremia and those with serious underlying disease.

PROSPECTIVE SURVEILLANCE OF NOSOCOMIAL INFECTION AT THE SECURITY FORCES HOSPITAL, RIYADH, EI Sobayo, Q Haddad, Security Forces Hospital, Riyadh

Infection surveillance activities represent the core of a hospital infection control program for the early detection of clusters of infections. This in turn leads to immediate implementation of appropriate control measures to contain infection spread. Security Forces Hospital is a 300-bed acute care facility. Clusters of *Pseudomonas aeruginosa* of about the same sensitivity pattern were isolated from surgical wounds, urine, and sputum of inpatients in surgical and medical areas of the hospital between 7 and 28 February 1989. Epidemiological investigation was carried out to identify sources of the infection or any reservoir that may cause continued spread of the organism. Thirty-two random samples from some environmental objects suspected to be reservoirs of infections were investigated bacteriologically. Staff in the operating room were also investigated. Six samples (19%) from all sources showed colonization with *Pseudomonas aeruginosa* of a similar sensitivity pattern. Hospital-associated infections for the period under discussion showed the predominant organisms causing infections and the service areas the organisms were associated with. Wound infection was also classified. Overall infection rate was 2.0%. Implementation of appropriate measures eradicated *Pseudomonas aeruginosa* from the incriminated environmental objects.

TUBERCULOSIS: A PUBLIC HEALTH PROBLEM AMONG AFGHANI REFUGEES, JS Jarallah, S Al-Shammari, J Faqiha, Department of Community and Family Medicine, King Saud University, Riyadh

Tuberculosis is a known disease problem among refugees where there is overcrowding and malnutrition. To study the clinical and some epidemiological patterns of tuberculosis among Afghani refugees, a retrospective review was done of 420 patients who attended a tuberculosis center in Quetta, Pakistan. 52.6% of the cases were males and 47.4% were females. Average age was 29.8 ± 16.8 years and the average number per household was 7.3 ± 3.26 persons. In 28% of the cases, another member of the family was known to have TB. The most frequent symptom was fever (93.1%), cough (92.4%), night sweats (83.1%), sputum (75.9%), and only 25.5% had hemoptysis. The most frequent finding on a chest x-ray study was calcification (27.1%), fibrosis (15.7%), and only 8 patients had cavitation. 100 patients (23.8%) had extrapulmonary tuberculosis (lymphadenitis, 37; skeletal affliction, 55; and genitourinary affliction, 8). It was proposed to treat all cases for a minimum of 8 months using different regimens, as recommended by the WHO. Only 62.6% had completed the course, while 8% were defaulters and 4.6% were lost to follow up. Evidence of drug toxicity was observed in only 3 patients. Only 29 patients received BCG vaccine. Although the provision of drugs is excellent in the centre, there is a lack of contact tracing, and difficulties in motivating patients to complete treatment needed to be overcome. The status of BCG vaccination among the refugees in the camps should be improved.

BRUCELLOSIS: ANTIMICROBIAL THERAPY AND OTHER ASPECTS OF DIAGNOSIS AND TREATMENT, EJ Young, Baylor College of Medicine, Houston, Texas, U.S.A.

Brucellosis in domestic and semidomestic animals remains a prevalent zoonosis in many areas of the world, especially in developing nations. Human infection is related to the prevalence of brucellosis in animals, standards of veterinary and community health practices, and customs relative to animal husbandry and the preparation of food. A variety of new antimicrobial agents such as trimethoprim/sulfamethoxazole, rifampin, the quinolones, and some third-generation cephalosporins have potent in vitro activity against *Brucella*. Clinical experience with these agents in large numbers of patients is somewhat limited, and in some cases in vitro results do not parallel expectations from in vitro findings. The tetracyclines, especially doxycycline, with or without concomitant aminoglycoside antibiotics, remain the standard of treatment for human brucellosis, and appear to be associated with the lowest rates of relapse. With regard to diagnosis, a variety of new serological techniques are now available, including radioimmunoassay (RIA) and enzyme-linked immunosorbent assays (ELISA). Although these techniques appear to be more sensitive than agglutination tests, the serum agglutination test (SAT) and the 2-mercaptoethanol (2-ME) agglutination test remain the standards against which other methods are compared. In the author's opinion, far too much emphasis has been placed on the clinical entity called "chronic brucellosis." When cases of so-called chronic brucellosis were studied in detail, analyzing historical, epidemiological, and serological information, the incidence of chronic brucellosis was found to be extremely low. Nevertheless, delayed convalescence from acute brucellosis occurs with significant frequency and presents a diagnostic and therapeutic dilemma for physicians caring for patients with brucellosis.

INFECTION OF PROSTHETIC DEVICES, EJ Young, Baylor College of Medicine, Houston, Texas, U.S.A.

The ability to replace diseased organs and tissues with prosthetic devices is a major accomplishment of modern medicine, and the number and complexity of such devices continue to increase. Many prosthetic devices are implanted permanently, some are used for short periods, and still others are used to bridge the period from organ failure to transplantation of a donor organ. Infection is a rare but potentially lethal complication of prosthesis surgery. Microorganisms commonly involved in prosthesis infections, such as coagulase-negative staphylococci, are often of low pathogenicity for the normal host. The implantation of commonly used devices, such as joint prostheses, has doubled over the past ten years, and this trend continues. Prosthesis-related infections add appreciably to the cost of medical care, are a source of significant morbidity, and occasionally mortality. Despite advances in developing biomaterials with low reactivity in host tissues, infection at the tissue/prosthesis interface is the major limiting factor in the replacement of diseased or damaged organs. The use of prophylactic antibiotics in implant surgery is complicated by the resistance patterns of organisms commonly encountered, and by the emergence of multiply resistant strains. Careful selection of candidates for prosthesis surgery, eradication of preexisting foci of infection, and strict adherence to aseptic techniques remain the most effective methods to prevent prosthesis-related infections. Aspects of diagnosis and treatment of prosthesis-related infections was discussed.

A COMPARATIVE STUDY OF HEPATITIS B-SURFACE ANTIGEN REACTIVITY IN MALE BLOOD DONORS IN RIYADH, MA Kamel, HO Ezzat, W El-Karamany, MO Zayed, M Abdel Gamal Eldin, AZ Al-Drees, Forensic Medicine and Clinical Toxicology Department, Faculty of Medicine, Ain Shams University, Abbassiah, Cairo, Egypt

The objective of this study was the chronological assessment of the HBs prevalence of reactivity in the male blood donors of Riyadh Central blood bank during five years, analyzed according to nationality and age incidence. A trial was undertaken to reveal any relationship of the HBV reactivity to the main blood groups. The sensitive third-generation tests were employed, mainly the RPHA & the ELISA. The total cases examined were 113,149. It was evident that the percentage of reactivity in Saudi Arabians has progressively decreased from the year 1405 (7.5%) to the low level of 4.1% in 1408. The seropositivity of 4.5% in expatriates in the same year was higher. Regarding expatriates, the Africans and Yemenis have the highest prevalence. In order of incidence, donors of the blood group O, A, B, and lastly AB showed almost the same HBs predilection. The Rh-positive predilection was the same in both Saudi Arabians and expatriates, but was less in the Rh-negative in the latter. The prevalence of viral hepatitis in Riyadh, in all considerations, is parallel to that in other parts of the world. This diminishing prevalence points to improved hygienic and socioeconomic conditions in those countries with the highest standards of health development.

DRUG RESISTANCE AND ITS INFLUENCE ON RESPONSE TO SHORT-COURSE CHEMOTHERAPY OF TUBERCULOSIS, IO Al-Orainey, College of Medicine, King Saud University, Riyadh

Clinical trials of short-course chemotherapy were evaluated to assess the influence of drug resistance on response to therapy. The failure rate among patients with sensitive strains ranged between 0 and 30%, depending on the type and number of drugs used and duration of therapy. Patients with resistant strains had a failure rate of 0 to 75%. Regimens containing both rifampicin and pyrazinamide gave the best results, with low failure rates among both sensitive and resistant strains. In fact, resistance to streptomycin and isoniazid had very little influence on response in regimens containing this combination. The addition of streptomycin or ethambutol to the above regimen also did not influence the response. Non-rifampicin–containing regimens were associated with high failure rates, particularly in patients with resistant strains. Prolonging the duration of therapy was generally associated with a better response. However, in rifampicin-containing regimens the use of pyrazinamide beyond 2 months did not influence the outcome of therapy. The inclusion of rifampicin and pyrazinamide in short-course therapy regimens minimized the influence of drug resistance on response to therapy. This probably will continue to be true as long as rifampicin resistance remains at very low levels.

STRONGYLOIDES HYPERINFECTION SYNDROME: A CASE REPORT FROM TAIF, AM Imam, King Faisal Hospital, Taif

Strongyloidiasis is a human intestinal parasitosis caused by the round worm *Strongyloides stercoralis*. Strongyloides hyperinfection syndrome (SHS) results from autoinfection and dissemination of the parasite into extraintestinal organs (e.g., brain and lungs). SHS is rare and is seen in debilitated or immunocompromised patients and in those who receive immunosuppressive agents. In this communication we report SHS in a 60-year-old female patient. She has been a known hypertensive for 15 years. She had had body itch for 6 months. Stool examination was negative and she was given antihistaminics. Next, steroids were added as her body itch did not subside and the patient showed only temporary improvement on steroid therapy. Two months later the patient sought medical advice again and stool examination showed *Strongyloides stercoralis* larvae. Antihelminthic treatment was given with good but temporary response. We saw the patient one year after the onset of her symptoms and stool examination showed heavy strongyloidiasis. In view of the patient's age, medical history of hypertension, generalized body itch, history of steroid therapy, signs of linear skin lesions caused by migrating larvae, and positive stool examination the diagnosis of SHS was established. The patient was started on thiabendazole, 25 mg per kilogram of body weight twice daily for 10 days. This treatment course was repeated monthly for 3 months. The patient showed marked gradual improvement and ultimately became asymptomatic. An uneventful outcome in SHS depends on early diagnosis and proper full treatment, as reported recently. Fatalities, not uncommon in SHS, are usually due to peritonitis secondary to perforated bowel, or due to brain damage or respiratory failure. We think that a positive laboratory report indicating strongyloidiasis should prompt the clinician to exclude SHS in candidate patients.

GIARDIASIS: BETTER DIAGNOSIS FOR COMMON PARASITE, MH Al-Tukhi, Security Forces Hospital, Riyadh

Giardiasis is reported to exist throughout the Kingdom of Saudi Arabia, from different sources. The infection rate reported from the three main hospitals in the Riyadh area varies between 14 and 86%. It is considered to be the most prevalant of gut parasites. Sex, age, and nationality are factors that play roles in the prevalence of giardiasis. Water supply can be a source of infection in many areas. ELISA has been evaluated for the detection of antibodies to *G. lamblia* antigen in sera from infected and noninfected populations in the Riyadh area. Sensitivity was 86% and specificity was 85%.

BRAIN ABSCESS DUE TO STREPTOCOCCUS MILLERI IN SAUDI ARABIA, AM Al-Rasheed, AR Choudhury, S Bakheshwain, F Bartlett, KR Al-Moutaery, AO Osoba, Armed Forces Hospital, Riyadh

It is now well established that *Streptococcus milleri* is a virulent causative agent of abscesses, not only in the brain, but also in the liver, lung, and appendix. We present two cases of brain abscess due to *S. milleri*. The first case was in a 4-year-old boy who was initially started on antibiotherapy and the abscess subsequently excised, resulting in full recovery. The second case was in a 38-year-old man with a previous history of tuberculosis. A CT brain scan showed frontal and parietal abscesses. Anti-TB therapy initiated because of the history produced no clinical improvement. Surgical excision followed by appropriate antibiotherapy produced clinical recovery. *S. milleri* organisms were isolated from the brain abscess material in both cases, and were identified by standard bacteriological procedures. The pathogenesis and management of these cases were discussed and suggestions made for the initial therapy pending bacteriological diagnosis. As far as we are aware, this is the first case of this organism causing brain abscess reported from Saudi Arabia.

ACUTE MENINGOCOCCAL MENINGITIS IN MAKKA CHILDREN, JO Al-Labadi, A Tashkandi, King Faisal Hospital, Makka

One hundred sixty-six cases of meningococcal meningitis in children were admitted to King Faisal Hospital during the 1987 Hajj period. The mean ages of patients was 5.3 years (+ 1.5 SD); 58% were male, 58% were residents. 94% were admitted after 9 Dhu Al Hijja. The mortality rate was 5%. Their nationalities, clinical picture, date of admission, serum electrolytes, renal function tests, blood glucose, hemogram, and CSF examinations were evaluated. All received penicillin G in the standard dose intravenously. There was a significantly high frequency ($0.01 > P > 0.001$) of 6 clinical and 4 laboratory findings in death cases. These were: younger than 3 years; coma; rectal temperature, > 39.5°C; systolic blood pressure, < 70 mm Hg; presence of purpuric rashes; respiratory rate, > 30/min; leukocyte count,10 × $10^3/\mu l$; platelet count, < 150 × $10^3/\mu l$; blood pH, < 7.30; serum bicarbonate, < 15 mEq/L; and serum creatinine > 130 μmol/L on admission. The constructed prognostic score shows that all patients with a score of greater than 6 died, so one can base one's prognosis solely on the presence of the clinical factors.

Announcements

The *Annals of Saudi Medicine* is pleased to publish announcements of educational opportunities of interest to its readers. For adequate publicity, notices of postgraduate courses, meetings, and lectures must be received at least 6 months before the date of occurrence. Please send relevant information to the *Annals of Saudi Medicine*, Publications Office, King Faisal Specialist Hospital and Research Centre, P.O. Box 3354, Riyadh 11211, Saudi Arabia.

King Saud University Fellowship in Pathology

King Saud University announces the inception of a 5-year joint fellowship training program in pathology. The training will be at King Khalid University Hospital, King Faisal Specialist Hospital and Research Centre, and Riyadh Armed Forces Hospital, and is a full-time program. Application is open to interested and suitably qualified residents from all over the Kingdom. To be eligible, applicants will meet the following criteria:

1. Doctors who hold MB,BS from King Saud University or equivalent degree with at least Good grade.
2. Doctors who have finished their internship in a recognized hospital with at least a Very Good grade.
3. Successful completion of a selection examination and personal interview.
4. Applicants from other institutions should submit a letter from his/her employer that he/she will be sponsored during the whole period of training.

Applications and inquiries should be sent to the Director, Postgraduate Medical Education, College of Medicine, King Saud University, P.O. Box 2925, Riyadh 11461, Saudi Arabia.

King Faisal Specialist Hospital and Research Centre Postgraduate Training Programs

King Faisal Specialist Hospital and Research Centre is pleased to invite applications for the following full-time postgraduate training programs:

1. Arab Board residency training in the specialties of internal medicine, obstetrics/gynecology, pediatrics, and surgery.
2. Five-year pathology residency training program, affiliated with the Royal College of Pathologists of Australasia and the King Saud University.
3. Fellowships, both adult and pediatric, in cardiology, endocrinology, gastroenterology, infectious diseases, nephrology, hematology, and oncology. Also, adult pulmonary and critical care medicine, adult rheumatology, pediatric allergy and clinical immunology, neonatal/perinatal medicine, and pediatric neurology.

For further information contact the Director, Academic Affairs and Postgraduate Education, King Faisal Specialist Hospital and Research Centre, P.O. Box 3354, Riyadh 11211, Saudi Arabia; telephone (01) 464-7272, extension 1837.

Radiopharmaceuticals from King Faisal Specialist Hospital and Research Centre

King Faisal Specialist Hospital and Research Centre manufactures various radiopharmaceuticals at its Radionuclide and Cyclotron Operations facility with the aid of model CS-30 Cyclotron. These radiopharmaceuticals are produced according to international standards of good manufacturing practice. The Research Centre meets the high standards of quality assurance and environmental safety with regard to radiopharmaceuticals.

Radiopharmaceuticals currently produced and available for distribution throughout the Kingdom and to adjoining Arab states are as follows: thallous (Tl-201) chloride injection ($T^{1}/2$ = 73 h); gallium (Ga-67) citrate injection ($T^{1}/2$ = 78.3 h); iodine-123 capsules ($T^{1}/2$ = 13.1 h); iodine-123 oral solution ($T^{1}/2$ = 13.1 h); iodine-123 orthoiodohippurate solution ($T^{1}/2$ = 13.1 h); rubidium (Rb-81) → krypton (Kr-81 m) generator ($T^{1}/2$ = 4.58 h – 13 s); indium (In-111) oxine ($T^{1}/2$ = 67.92 h) for cell labeling; indium (In-111) DTPA for cisternography ($T^{1}/2$ = 67.92 h).

Suggestions from the medical community for additional cyclotron-produced needs are welcome.

Inquiries concerning the availability, price schedule, and technical information on specific radiopharmaceuticals should be directed to: Abbass H. Al-Marzouky, MD, Executive Director, Research Centre, King Faisal Specialist Hospital and Research Centre, P.O. Box 3354, Riyadh 11211, Saudi Arabia (Fax No. 966-1-441-4839).

Joint Board for Postgraduate Medical Education Symposia for 1411

The Joint Board for Postgraduate Education is pleased to announce the following symposia for 1411.

1. Postgraduate and Continuing Medical Education; College of Medicine, King Saud University, 21-22 Shawwal 1411 (5-6 May 1991).

For further information, contact the Joint Board Office, College of Medicine, King Saud University, P.O. Box 2925, Riyadh 11461, Saudi Arabia; telephone (01) 467-1556 or 1564; telefax 481-1853; telex 403748 DARAYAH SJ.

King Faisal Specialist Hospital and Research Centre Symposia for 1411

King Faisal Specialist Hospital and Research Centre is pleased to announce the following educational activities for 1411.

1. FMGEMS Examination; 12–13 Muharram 1412 (23–24 July 1991)

For further information, contact Academic Affairs and Postgraduate Education, King Faisal Specialist Hospital and Research Centre, P.O. Box 3354, Riyadh 11211; telephone 464-7272, extension 1865 or 1834, fax 442-7237.

*Sponsored by the Joint Board for Postgraduate Medical Education.

Residency Training Programme in Orthopaedics

The regional office of the Arab Board (Joint Board) announces the schedule of new intakes for the orthopaedic residency training programme (Arab Board Certificate in Orthopaedics) commencing Ramadan 1411 A.H./April 1991 A.D. in the following hospitals in Riyadh: Armed Forces Hospital, Riyadh Central Hospital, King Fahad National Guard Hospital, King Faisal Specialist Hospital, King Khalid University Hospital, Security Forces Hospital.

Requirements: Graduate from a recognized medical school and completion one one-year postgraduate internship to commence the five-year-residency training programme in surgery and orthopaedics.

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Holder of the Arab Board Part 1 in surgery to commence the three year residency training programme in orthopaedics. Capable of speaking and writing in Arabic and English.

Applications are being accepted now! Deadline for submissioin is 30 Rajab 1411 (14 February 1991).

Application forms are available from and should be submitted to: The Co-ordinator, Arab Board Orthopaedic Residency Programme, Security Forces Hospital, P.O. Box 3643, Riyadh 11481, Tel: 477-4480, Ext.: 1371.

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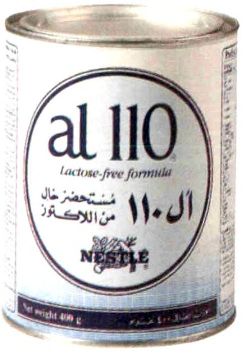

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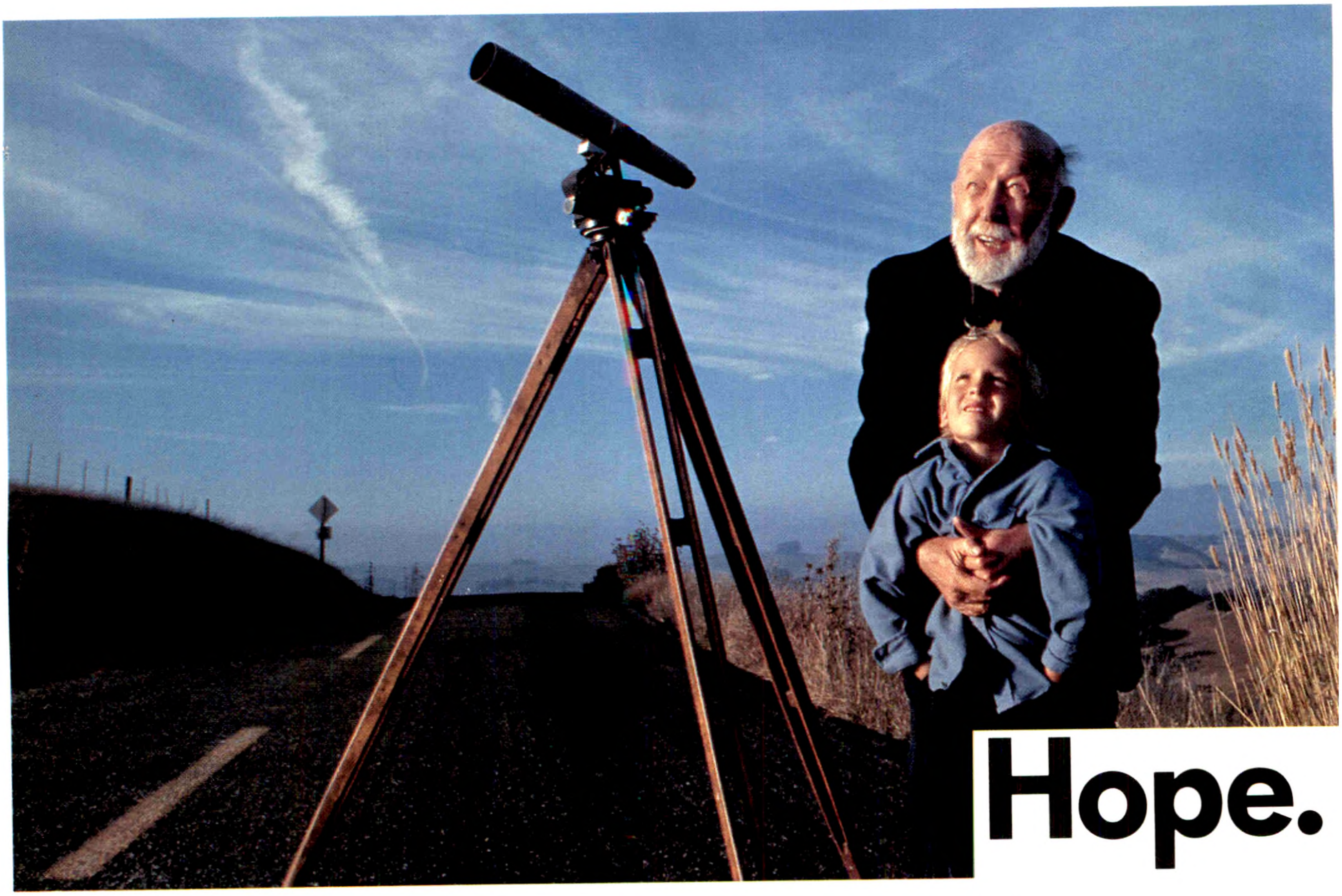

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Title Page. The title page must contain (1) title of the article, (2) correct names of each author plus highest academic degree for each, (3) each author's official academic and/or clinical title and affiliation, (4) name and address of the institution(s), (5) name and address of author to whom correspondence should be sent, if it differs from the first author, and (6) any disclaimers. For case reports, it is recommended that the number of authors be limited to four. Acknowledgment of support should be included in the Acknowledgment section at the end of the article.

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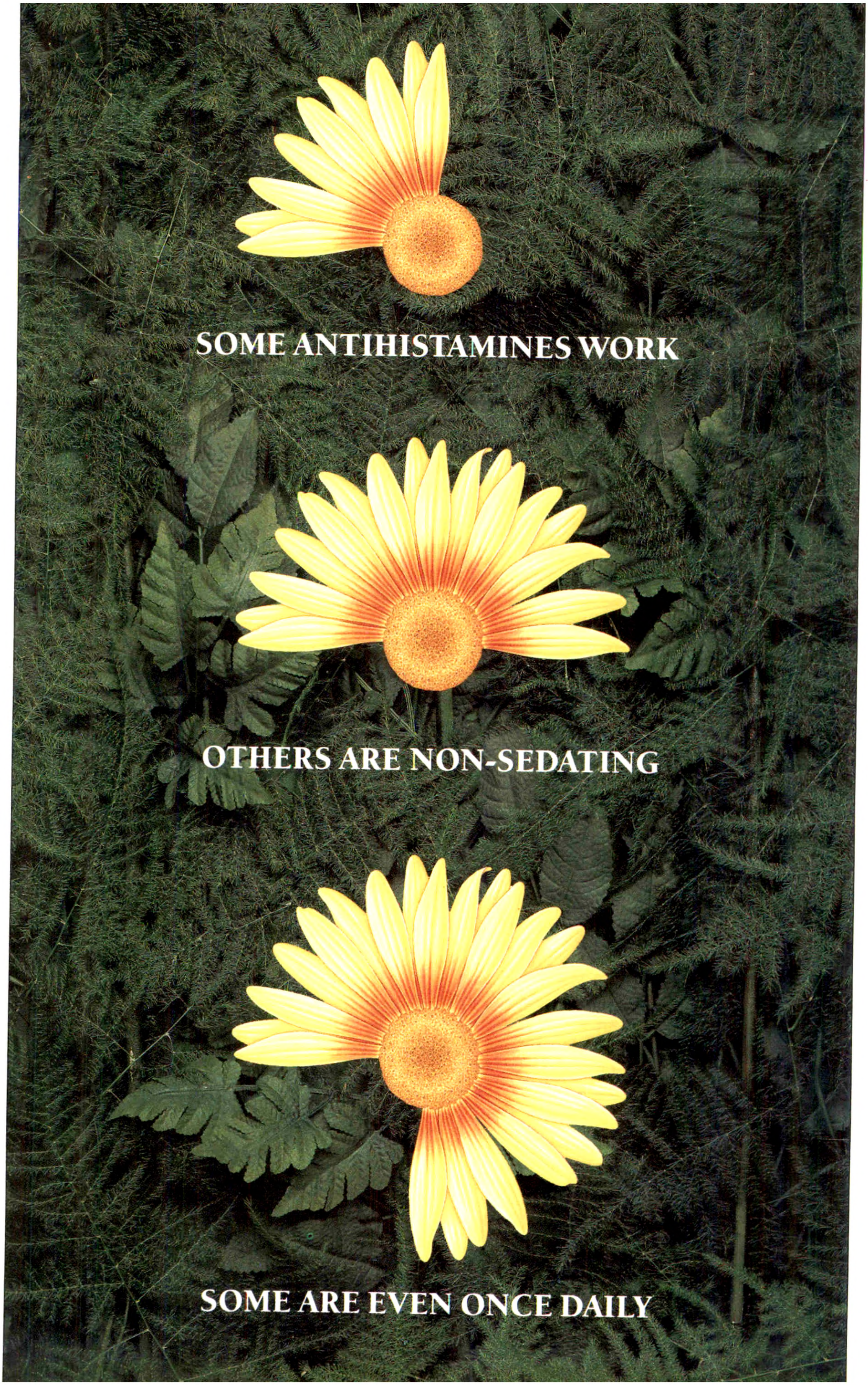
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SOME ARE EVEN ONCE DAILY

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مساعدتا التحرير:

فرجينيا جي كروزير
شيرلي موفيت

المدونات الطبية السعودية مجلة تنشر بموجب الأمر الملكي السامي رقم ٥/م/٢٤٢٢٣ بتاريخ ١٤ شوال عام ١٤٠٠هـ. وتصدر مرة كل شهرين، وهي مشروع مشترك بين كل من كلية الطب ومستشفى الملك خالد الجامعي ـ جامعة الملك سعود، صندوق بريد ٢٩٢٥ ـ الرياض ١١٤٦١، المملكة العربية السعودية، ومستشفى الملك فيصل التخصصي ومركز الأبحاث، صندوق بريد ٣٣٥٤ ـ الرياض ١١٢١١، المملكة العربية السعودية. يتم صف وطبع المجلة بمطابع جامعة الملك سعود. يتم توزيع المدوَّنات بواسطة قسم البريد التابع لإدارة الخدمات الإدارية بمستشفى الملك فيصل التخصصي ومركز الأبحاث. كما يتولى قسم الترجمة في هذه الإدارة إعداد الملخصات العربية بالاشتراك مع الدكتور محمد زهير القاوي. كل المراسلات والاستفسارات وطرق الحصول على المستلات ترسل إلى مكتب المطبوعات على العنوان التالي:

مكتب المطبوعات
مدونات الطب السعودي
مستشفى الملك فيصل التخصصي ومركز الأبحاث
ص. ب ٣٣٥٤
الرياض ١١٢١١ ـ المملكة العربية السعودية

مندوب الاعلانات
بي آر سي المتحدة
ابسوم ـ سري ـ المملكة المتحدة

الآراء التي ترد في المقالات المنشورة تعبر عن رأي أصحابها فقط ولا تعبر عن وجهة نظر مجلة المدونات الطبية السعودية. لا يسمح بإعادة طبع أي جزء من المجلة أو نسخه بأي شكل وبأي وسيلة سواء أكانت إليكترونية أو آلية، بما في ذلك التصوير والتسجيل أو الإدخال في أي نظام حفظ أو استعادة معلومات إليكتروني، بدون الحصول على موافقة مسبقة من إدارة المجلة.

Claritine is an outstanding new antihistamine that combines
all the benefits of other antihistamines.
Firstly, Claritine is really effective in both allergic rhinitis and allergic skin disorders.
Secondly, it is truly non-sedating with absolutely no CNS effects.
It also has a convenient once daily dosage that controls symptoms for the full 24 hours.
Finally Claritine has something extra, which makes it special.
It starts relieving symptoms within 30 minutes, a speed no other antihistamine can match.
With all these advantages Claritine adds up
to a superior antihistamine that outperforms the rest.

CLARITINE*
LORATADINE

AS GOOD AS THE BEST, FASTER THAN THE REST

CLARITINE* TABLETS Brand of loratadine. Long-Acting. Non-Sedating Antihistamine. **DESCRIPTION** Each CLARITINE Tablet contains 10 mg micronized loratadine and the inactive ingredients starch, lactose and magnesium stearate. **ACTIONS** Loratadine is a potent long-acting tricyclic antihistamine with selective peripheral H_1-receptor antagonistic activity. **INDICATIONS AND USAGE** CLARITINE Tablets are indicated for the relief of symptoms associated with allergic rhinitis, such as sneezing, nasal discharge (rhinorrhea) and itching, as well as ocular itching and burning. Nasal and ocular signs and symptoms are relieved rapidly after oral administration. CLARITINE Tablets are also indicated for relief of symptoms and signs of chronic urticaria and other allergic dermatologic disorders. **DOSAGE AND ADMINISTRATION Adults and children 12 years of age and over:** one CLARITINE Tablet once daily. **DRUG INTERACTIONS** When administered concomitantly with alcohol, CLARITINE Tablets have no potentiating effects as measured by psychomotor performance studies. **Drug/laboratory test interactions:** Antihistamines should be discontinued about four days prior to skin testing procedures since these drugs may prevent or diminish otherwise positive reactions to dermal reactivity indicators. **ADVERSE REACTIONS** During controlled clinical studies, the incidence of adverse effects associated with 10 mg CLARITINE Tablets treatment was comparable to that associated with placebo. In these trials, loratadine showed no clinically significant sedative or anticholinergic properties since fatigue, sedation, headache and dry mouth were rarely reported events and frequency of these effects for both loratadine and placebo was not statistically different. Nausea was also rarely reported. **CONTRAINDICATIONS** CLARITINE Tablets are contraindicated in patients who have shown sensitivity or idiosyncrasy to their components. **PRECAUTIONS** Safety and efficacy of CLARITINE Tablets in children younger than 12 years of age have not yet been established. The safe use of CLARITINE Tablets during pregnancy has not been established and therefore, the compound should be used only if the potential benefit justifies the potential risk to fetus. Since CLARITINE Tablets are excreted in breast milk, caution should be exercised when CLARITINE Tablets are administered to a nursing woman. **HOW SUPPLIED** In packs of 10 and 30 tablets. Store between 2 and 30°C. *Trademark, Schering Corporation, Kenilworth, New Jersey. U.S.A. SCHERING CORPORATION U.S.A. KENILWORTH, NEW JERSEY.

ANISTREPLASE

EMINASE

ANISOYLATED LYS-PLASMINOGEN STREPTOKINASE ACTIVATOR COMPLEX (APSAC)

PRESCRIBING INFORMATION

Presentation

EMINASE is supplied as a white to off-white sterile lyophilised powder in vials containing 30 Units of the p-anisoylated derivative of the primary (human) lys-plasminogen-streptokinase activator complex (APSAC; anistreplase) together with buffering and stabilising agents.

Indications

EMINASE is indicated in the treatment of acute myocardial infarction to establish reperfusion, preserve left ventricular function, limit infarct size and to reduce mortality.

Clinical studies have shown that EMINASE significantly reduces 30-day and 1-year mortality, limits infarct size and preserves left ventricular function.

Dosage and Administration

30 Units of EMINASE should be given as a single slow intravenous (IV) injection over 2-5 minutes. *Do not administer by intramuscular injection.*

EMINASE should be administered as soon as possible after the onset of symptoms of myocardial infarction.

See Package Insert Leaflet for details of preparation and administration.

Contra-Indications

Since thrombolytic therapy increases the risk of bleeding, EMINASE is contra-indicated in the following situations: 1. Surgery or major trauma within the previous 10 days. 2. Peptic ulceration, gastro-intestinal bleeding or other internal bleeding within the past 6 months. 3. Known bleeding diathesis. 4. History of cerebrovascular accident. 5. Severe, uncontrolled hypertension. 6. Known intracranial neoplasm or aneurysm. 7. Recent (within 2 months) neurosurgical procedure.

EMINASE should not be administered to patients who have experienced severe allergic reactions to this product or streptokinase.

Precautions and Warnings

Patients with any condition in which bleeding constitutes a significant hazard, or in which it would be particularly difficult to manage because of its location, should be monitored carefully. The risk associated with EMINASE therapy may be increased in such patients and should be weighed against the anticipated benefits.

Following administration of EMINASE, venepuncture and other invasive procedures should be kept to a minimum in order to reduce the risk of bleeding. In patients undergoing cardiac catheterisation, the catheter sheath should not be removed until 24 hours after dosing.

In the following conditions, the risks associated with thrombolytic therapy may be increased and should be weighed against the anticipated benefits: ● haemorrhagic diabetic retinopathy or other haemorrhagic conditions ● subacute bacterial endocarditis ● atrial or ventricular mural thrombosis, intracardiac tumours and aortic aneurysm ● septic thrombophlebitis or occluded AV cannula at a seriously infected site ● haemostatic defects including those secondary to severe hepatic or renal disease ● recent or current treatment with oral anticoagulants.

Hypotension, sometimes severe, has occasionally been observed soon after intravenous EMINASE administration. It is not recommended that EMINASE be administered rapidly (less than 2 minutes).

Re-administration

Because of the increased likelihood of resistance due to antistreptokinase antibody, EMINASE may not be effective if administered more than 5 days after prior EMINASE or streptokinase therapy, particularly between 5 days and 12 months. Furthermore, increased antistreptokinase antibodies after EMINASE or streptokinase may also increase the risk of allergic reactions following re-administration.

Elderly Patients

Experience is limited in patients over 75 years of age and the benefits of EMINASE should be balanced against risk in this group.

Adverse Events

Hypotension observed occasionally soon after EMINASE administration is usually transient and is often associated with bradycardia.

Early reactions of flushing and bradycardia (usually within the first hour) as well as fever and nausea/vomiting (usually within 6 to 24 hours) have been reported but are generally not severe.

"Allergic-type" reactions, including bronchoconstriction or anaphylaxis have been reported but are uncommon and usually transient. A purpuric rash has occasionally been reported. All cases recovered spontaneously without sequelae.

The most common complication associated with EMINASE, as with other thrombolytics, is bleeding, most frequently from arterial and venous puncture sites. Haemoptysis, haematuria, haematemesis and malaena have been reported occasionally. Cerebrovascular accidents have been reported but the incidence is low and there has usually been a predisposing factor.

Local bleeding can be controlled with pressure. In cases of severe, uncontrolled bleeding, tranexamic acid or aprotinin should be given by slow intravenous injection to stop the fibrinolytic activity of EMINASE. Additionally, cryoprecipitate, purified clotting factor concentrates or fresh whole blood may be used to correct the haemostatic deficiency. If the haematocrit has fallen significantly, a blood transfusion may be necessary.

Reperfusion-associated arrhythmias have been reported following EMINASE treatment. These are generally transient but if prolonged they can be controlled with appropriate therapy.

Availability

IV Injection Pack:

1 vial EMINASE 30 Units, a 5ml ampoule of Water for injections B.P., a 5ml disposable syringe and needle.

Storage and Stability

EMINASE should be stored in a refrigerator (2°-8°C) and must not be used after the expiry date printed on the pack and vial, EMINASE vials must not be stored at room temperature.

Further information is available on request.

EMINASE is a product of research from Beecham Pharmaceuticals, a part of SmithKline Beecham Pharmaceuticals, Brentford, England.

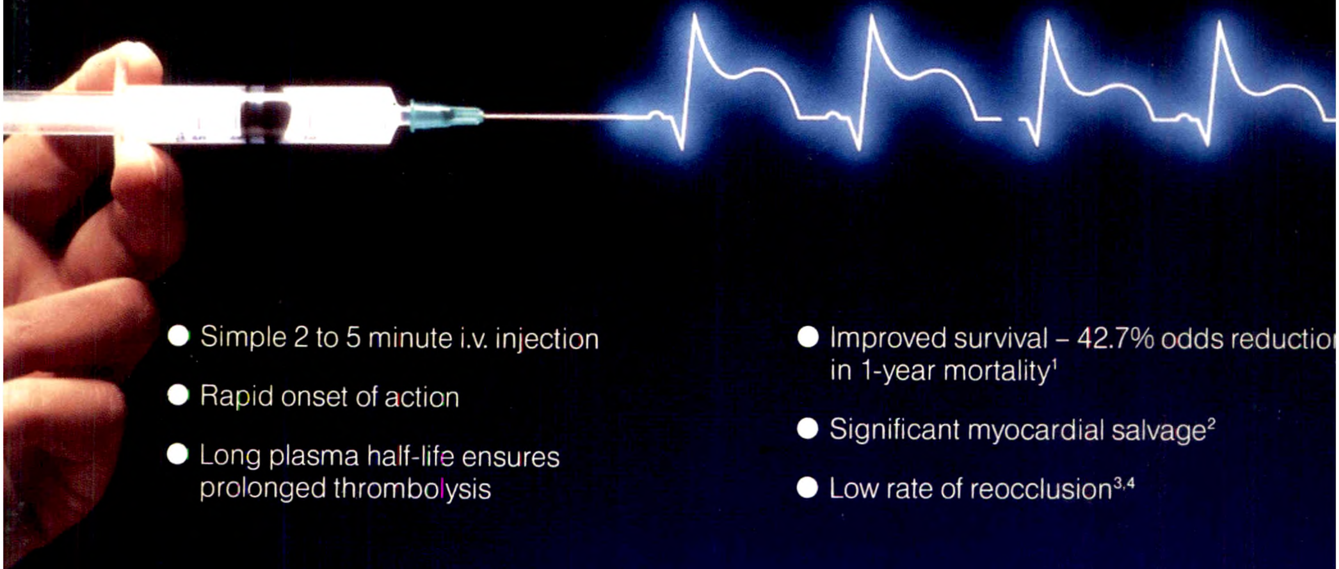
EMINASE and the cardiovascular logo are trade marks.

Prescribing Information revised November 1990. 488/EMI/01/90

SB

SmithKline Beecham
Pharmaceuticals

INJECT SURVIVE



- Simple 2 to 5 minute i.v. injection
- Rapid onset of action
- Long plasma half-life ensures prolonged thrombolysis

- Improved survival – 42.7% odds reductio in 1-year mortality[1]
- Significant myocardial salvage[2]
- Low rate of reocclusion[3,4]

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NEW
ANISTREPLASE
EMINASE
***A**NISOYLATED LYS-**P**LASMINOGEN **S**TREPTOKINASE **A**CTIVATOR **C**OMPLEX (APSAC)*
simply practical thrombolysi

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Pharmaceuticals

For prescribing information see overleaf.

488/EMI/01

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